BRAIN.

PART I., 1903.

Original Articles and Clinical Cases.

THE AUTONOMIC NERVOUS SYSTEM.

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Presidential Address.

I PROPOSE this evening to consider the general plan of the efferent system of nerves which controls the unstriated muscle, the cardiac muscle, and the glandular tissue of mammals; to point out very briefly how far this plan holds for other vertebrates; and to discuss the question of the existence of an afferent system of nerves corresponding to the efferent system.

Much that I have to say to you I have, at some time or other, already said, but I do not think I need apologise for giving you a general summary. The number of facts which have accumulated on these subjects is so vast that it is imperative to try and co-ordinate them. Every day results are published on quite trivial evidence because no general scheme is borne in mind, and because there is no standard of probability. Such results only serve to obscure the subject; if they were subjected to proper scrutiny, they might become valuable evidence for a general law.

Efferent Fibres.

The system of nerves with which we have to deal we may speak of as the *autonomic nervous system.*

Origin from separated portions of the central nervous system.—The efferent autonomic fibres leave the central nervous system in four regions, which are separated from one another by regions from which no efferent autonomic fibres pass. The four regions (*cf.* fig. 1) are (1) that underlying the anterior corpora quadrigemina, from which fibres pass by the ciliary nerves to the iris and ciliary muscle. This we may call the *mid-brain autonomic system.*

(2) The region a little above and below the calamus scriptorius, from which fibres pass by the seventh nerve —probably from the intermediate of Wrisberg — and by the glossopharyngeal and vagus nerves. This supplies the blood-vessels and glands of the mouth, pharynx, and nose, the walls of the œsophagus, stomach, small intestine, and part of the large intestine, with the glands belonging to them; and it supplies the trachea and lungs. It is thus in large part, if not wholly, a special nervous system for the mouth end of the gut and for the structures developmentally connected with it. It does not, so far as we know, supply blood-vessels below the thorax. It may be spoken of as the *bulbar autonomic system.*

These two I have for convenience placed together under the heading of the *cranial autonomic system*; it is, however, probable that the two in development have run an independent course.

(3) The third region is the middle portion of the spinal cord, viz., the first thoracic spinal segment to the fourth or fifth lumbar segments inclusive in the cat, and to the second or third lumbar segments inclusive in man. It gives origin to the efferent fibres of the *sympathetic system,* passing outwards by the white rami, a fact which the researches of Gaskell did so much to establish.

(4) The last region is that of the first to the third sacral segments in the cat, and the corresponding segments in other mammals. This gives rise to the pelvic nerve (nervus

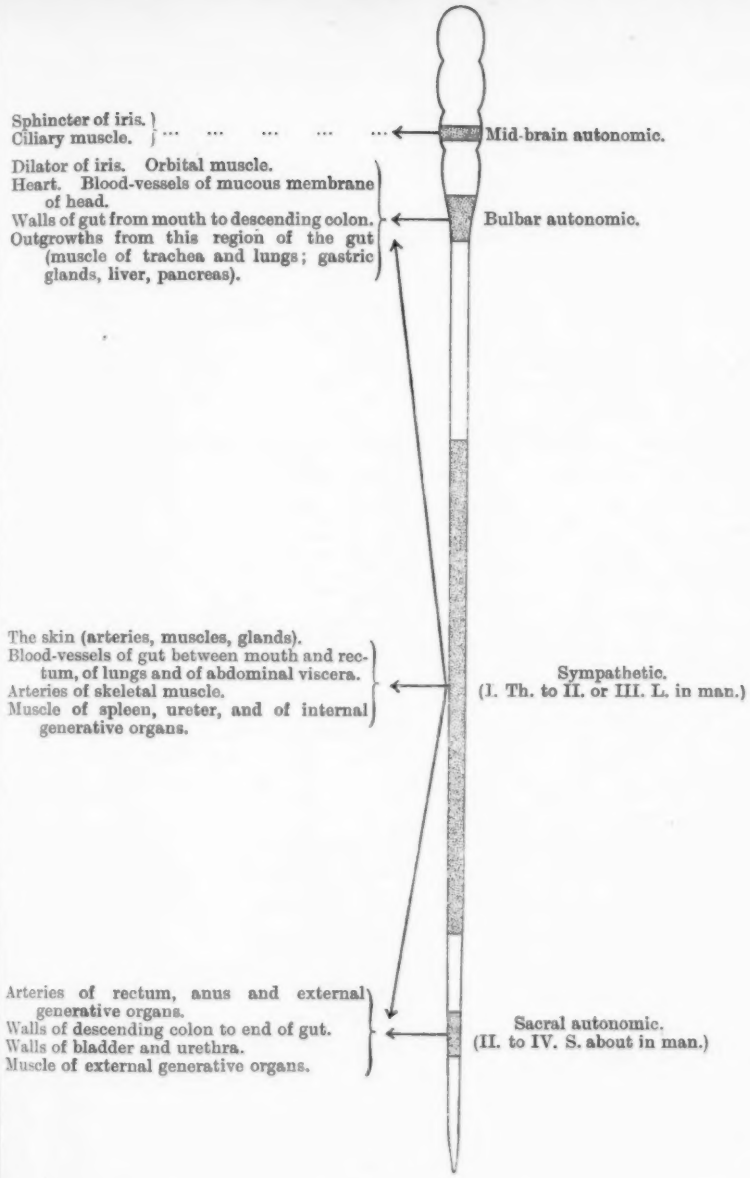
Sphincter of iris.
Ciliary muscle.
Mid-brain autonomic.
Dilator of iris. Orbital muscle.
Heart. Blood-vessels of mucous membrane of head.
Walls of gut from mouth to descending colon.
Outgrowths from this region of the gut (muscle of trachea and lungs; gastric glands, liver, pancreas).
Bulbar autonomic.
The skin (arteries, muscles, glands).
Blood-vessels of gut between mouth and rectum, of lungs and of abdominal viscera.
Arteries of skeletal muscle.
Muscle of spleen, ureter, and of internal generative organs.
Sympathetic.
(I. Th. to II. or III. L. in man.)
Arteries of rectum, anus and external generative organs.
Walls of descending colon to end of gut.
Walls of bladder and urethra.
Muscle of external generative organs.
Sacral autonomic.
(II. to IV. S. about in man.)

FIG. 1.

Diagram to show the general origin and distribution of efferent autonomic fibres. By "muscle" is, of course, meant unstriated muscle only. By the "walls" of a structure are meant all the unstriated muscle in it. The innervation in some cases is still a matter of controversy (gastric glands, liver, and pancreas; vessels of lungs; small arteries of skeletal muscles, and arteries of the central nervous system).

erigens) which supplies the walls of the anus, rectum and descending colon, the blood-vessels of the anus and rectum; the walls of the bladder, the substance and blood-vessels of the urethra and external generative organs. It is thus a special nervous system for the anal end of the gut and for the structures developmentally connected with it. This is the *sacral autonomic system.*

The view that efferent autonomic fibres do not arise from the regions left blank in the diagram is by no means universally accepted, but it is, I think, supported by all recent carefully conducted observations.

Question of independent development of the systems.—There are two obvious possibilities with regard to the local origin of the several autonomic fibres from the central nervous system. The nerve cells from which the fibres arise might be regarded as having been originally a continuous column of practically identical cells which in development have been separated from one another by the increase of other kinds of cells; thus the view has been taken that the central sympathetic cells have been separated on the one side from the central vago-glossophangeal cells by the development of the nervous system for the neck and fore-limbs, and on the other side from the central pelvic nerve-cells by the development of the nervous system for the hind limb.

The other possibility is that the cells of origin of the several systems have developed independently of one another in response to special conditions. On this view the bulbar and sacral autonomic systems are not to be regarded as separated parts of the sympathetic system, but as distinct systems having a different developmental history.

On comparing the bulbar autonomic, the sacral autonomic, and the sympathetic systems, we see that the first two have more in common with one another than either has with the sympathetic system. The bulbar and sacral systems are local in their supply; between them they send nerve fibres to the parts derived from the stomadæum, the proctodæum and the mesenteron, though they are not entirely confined to these parts. The sympathetic has also its local supply (body wall, limbs, kidney, internal generative organs),

but it sends nerve fibres also to all the parts which are supplied by the bulbar and sacral systems. Thus the tissues receiving efferent fibres from bulbar and sacral autonomic systems have a double nerve-supply, whilst the other tissues have but one. In the cases in which this double nerve-supply exists, the nerves coming from one system do not necessarily produce a different effect from that produced by the other; but, if the effect is different, then all the central nerve-strands of one system have one effect, and all the central nerve-strands of the other system have one and a different effect. Thus four or five spinal nerves send fibres by the sympathetic to the external generative organs, and each nerve causes contraction, and two or three spinal nerves send fibres by the sacral system to the external generative organs, and each nerve causes relaxation.

For these and other reasons I have advocated the view that the cranial and sacral autonomic systems are not simply separated parts of the sympathetic system, but that they are independent nervous developments with a different history. I do not, however, doubt that they have developed from homologous parts of the central gray matter.

But whilst I think that the three systems have had an independent development and should be regarded as separate systems, they have a number of features in common.

First fundamental point of resemblance of the several systems.—(1) No efferent autonomic fibre runs from the central nervous system to muscle or gland without having a nerve-cell in its course. In other words, the nerve-fibres which leave the central nervous system are all pre-ganglionic fibres; they end in connection with nerve-cells in the ganglia, and these give off post-ganglionic nerve-fibres which end in the tissues.

This deduction rests upon a large number of experiments with nicotine and by the degeneration method; but the fundamental experiment is that of stimulating the various parts of the central nervous system in a rabbit after 20 or more milligrams of nicotine have been injected intravenously. The stimulation causes no change of blood pressure, no contraction or relaxation of viscera, no secretion or

other effect. But on stimulating peripherally some one or other ganglion every autonomic effect can be obtained. A similar experiment made on the cat gives similar results; but the minimal amount of nicotine required is larger.

Limitations in the value of the nicotine method.—I wish once more to insist on certain limitations to the value of nicotine as indicating the presence and position of peripheral nerve-cells on pre-ganglionic fibres. It is the more important to do this because a most valuable method may easily be discredited if too much is expected of it and it is then found that it does not do what it has been said to do. The fact is that nicotine has in different animals a very unequal paralysing action on the peripheral ganglia.[1] In some animals, even in large doses, it only weakens the passage of nervous impulses, and this weakening may be of a very temporary nature. This can be shown by stimulating the peripheral end of a cut spinal nerve; a dose per kilogram which in one animal abolishes all trace of effect will in another animal leave the effect undiminished. There is a marked difference in the paralysing action of nicotine in the cat and dog; in two animals so closely related it is incredible that the arrangement of the nervous system should be so fundamentally different that in the one all efferent fibres have peripheral nerve-cells on their course, and in the other a large number of fibres should run direct to the tissue. It follows, then, that the nerve-cells are unequally affected by the drug in the two cases.

It may, however, be said that it is equally incredible that in two animals so closely related as the cat and the dog the nerve-cells or their endings should react so differently to nicotine. But in fact this presents no grave improbability. The reaction to nicotine no doubt depends upon the presence of a special chemical substance in the nerve-cells or on the nerve-endings. Although there are certain fundamental resemblances in the chemical constitution of protoplasm in the cat and dog, differences must of course exist.

[1] It is not yet certain whether the paralysing effect of nicotine occurs in consequence of an action on the endings of the pre-ganglionic nerve-fibres or on the substance of the nerve-cells.

And the recent investigation upon toxins and anti-toxins show what enormous effects on the organism these differences in chemical constitution may bring about.

Further, a difference in the behaviour to nicotine may occasionally be found in different individuals of the same species. The rabbit is very sensitive to nicotine; in numerous experiments I have found the passage of nerve-impulses to be stopped by a moderate dose of nicotine. But in one case, and in one only, large doses failed to produce paralysis. For some reason, to which I have no clue, the animal was immune. Lastly, different ganglia in any one animal are unequally affected; thus the ganglia of the solar plexus are less affected than the superior cervical ganglia or the ganglia of the lateral chain. Unless the nicotine when injected into the body puts an end to the autonomic effect of stimulating the cut anterior roots, the greatest caution must be exercised in drawing any conclusion as to the presence or absence of nerve-cells upon the efferent nerve-fibrēs. The decisive experiment in such cases must come by the use of the much more troublesome degeneration method.

The ganglia as groups of cells for particular areas.—The nerve-cells which are present on the course of the pre-ganglionic fibres might conceivably be arranged in groups according to their function, so that, for example, one ganglion might subserve vaso-dilator and another vaso-constrictor functions. I do not find that such an arrangement ever occurs in ganglia large enough to be readily seen by the eye, but it is possible that when the ganglia are small, as in a plexus, there may be considerable separation into groups of different function. Essentially the ganglia of each system are collections of nerve-cells for definite areas and each ganglion supplies all the kinds of nerve-fibres which are supplied to that area by the system to which it belongs.

Position of the ganglia in relation to their peripheral distribution.—The ganglia of the cranial and sacral autonomic systems are, broadly speaking, placed near the tissue which they supply, and for my present purpose I need not say more about them. The ganglia of the sympathetic

system supply the body wall and limbs as well as the viscera; there are some general features in the arrangement of these and of the fibres given off by them which it is worth while to point out.

The sympathetic ganglia are commonly divided into vertebral and pre-vertebral ganglia, but this division has a very imperfect correspondence with the distribution of the fibres they give off. Some of the vertebral ganglia send all or nearly all their fibres to the body wall or limbs; some send all their fibres to the viscera; some send fibres both to the body wall or limbs and to the viscera. In other words, in certain regions the separation of the nerve-cells which supply the body wall from those which supply the viscera has not taken place. The solar ganglia and the inferior mesenteric ganglia are visceral ganglia; the ganglia of the lateral chain from about the fourth thoracic ganglion downwards are for the supply of the body wall; the stellate and cervical ganglia are partly for the viscera and partly for the body wall.

The sympathetic ganglia and the nerves given off by them are intimately connected with the arteries, and the fibres which run to the viscera run with the arteries, but all the fibres which run to the skin leave the arteries to run to the somatic nerves. The larger arteries receive some nerve-fibres direct from the ganglia, fibres which affect the larger arteries only.

Skin areas of successive gray rami and of successive lateral ganglia.—Not only do the sympathetic fibres leave the arteries to run to the spinal nerves, but their peripheral distribution corresponds in the main with that of the spinal nerve which they join. The extent of outspread of the fibres in the periphery may differ, thus in the skin of the body wall the sympathetic fibre of adjoining spinal nerves overlap, by about a millimetre only, whilst the sensory fibres, according to the researches of Sherrington, overlap by about one-half of an area, but the area of sympathetic supply always lies in the area of the somatic sensory supply. In the limbs, the areas of the sympathetic fibres running to the nerves which form the plexus widely overlap, as Türck and

Sherrington have shown, the somatic sensory fibres do; here the overlapping of sympathetic fibres is at least as great as that of the somatic sensory fibres.

Although each ganglion of the lateral chain sends the great majority of its fibres to the corresponding somatic nerve, some ganglia commonly send a few fibres (*cf.* dotted lines in fig. 2) to the nerve above, some send a few to the nerve below, and some send a few both to the nerve above and to the nerve below. Thus the band of skin governed by each ganglion is not only wider than the band of skin supplied by the gray rami of the corresponding

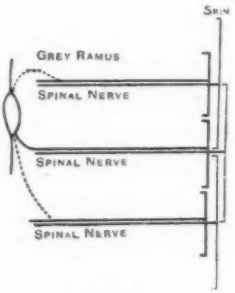

Fig. 2.

Diagram to show areas of skin of trunk supplied by three consecutive gray rami (thick brackets), and three consecutive spinal nerves (thin brackets). The thick brackets should overlap by about a millimetre. Also the distribution which sometimes occurs of the post-ganglionic fibres of single vertebral ganglion.

spinal nerve, but it may also be wider than the band supplied by the afferent somatic fibres of the nerve. It may be mentioned, however, that a ganglion rarely sends sufficient fibres to the nerve above or below its segmental nerve to supply the whole area; it usually supplies patches only in it.

Limits of the distribution of the sympathetic and of its various classes of fibres.—I have said that, broadly speaking, the sympathetic runs to all parts of the body, it does not by any means have an equal control of all parts. Its action may be very great, or it may be barely appreciable as in the case of the blood-vessels of the bladder. And although the

gray rami accompany the somatic nerves and the somatic nerves run both to skin and skeletal muscle, the rami cause great contraction of the small vessels of the skin, but cause little if any in the small vessels of the skeletal muscle; the decrease in blood supply to skeletal muscle which may be caused by sympathetic stimulation, seems to me to be mainly due to contraction of the larger arteries, though this has not been definitely shown. And there are other regions, for example, the region of distribution of the mid-brain autonomic nerves, in which it is doubtful whether the sympathetic has any effect.

A variation in the extent of the control of the sympathetic in different parts of the body is very generally recognised; but a variation in the kind of control is by many observers not accepted. Dastre and Morat have shown that the cervical sympathetic in the dog contains vaso-dilator fibres for the bucco-facial region, but it does not follow from this that vaso-dilator fibres accompany other vaso-constrictor nerves of the dog, and still less that they accompany the vaso-constrictor nerves of other animals. *A priori* it seems to me as likely that inhibitory nerves have developed in special tissues in response to special needs. The question is not one for generalisation but for experiment.

Other fundamental points of resemblance between the several systems.—Returning now to the common features of the cranial, sacral, and sympathetic nervous systems (*cf.* p. 5). They are:—

(2) Most, and probably all nerve-fibres which run from the central nervous system to a ganglion, *i.e.*, most, and probably all pre-ganglionic nerve-fibres divide into two or more nerve-fibres.

(3) Each branch of a pre-ganglionic nerve-fibre is connected with a nerve-cell.

(4) The axon given off by a nerve-cell, *i.e.*, the post-ganglionic nerve-fibre does not in any case run to another nerve-cell of the system, but runs to the peripheral tissue, branching as it goes so that it supplies a number of peripheral tissue-cells.

The element by the re-duplication of which the cranial and sacral autonomic and the sympathetic systems on the efferent side are made up, is, then, a spinal cord neuron and a group of peripheral neurons.

The afferent fibre I shall deal with presently, but in order to complete the general scheme I may add here that:—

(5) All the nerve-cells of the ganglia are on the course of efferent fibres, *i.e.*, the peripheral ganglia of these systems have no sensory nerve-cells in the ordinary meaning of the term. The afferent nerve-cells have their trophic centre in the spinal ganglia.

The connection of the axon of a spinal cell with a number of peripheral cells, each of which sends off an axon, explains

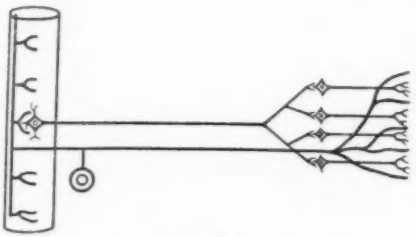

FIG. 3.

Diagram of elements of which the autonomic system is composed. The afferent nerves do not necessarily accompany the efferent nerves.

why more fibres leave a ganglion than enter it, a fact observed for certain ganglia by Bidder and Volkmann in 1848.

Anatomical basis for pre-ganglionic axon reflexes.—The peripheral neurons connected with a given spinal neuron are not necessarily all in one ganglion. In the superior cervical ganglia they are, but in most of the ganglia of the lateral chain of the sympathetic they are not, they are connected with three, four or more ganglia (*cf.* fig. 4).

This fact affords the explanation of nearly all the "reflex" actions which have been described as occurring in peripheral ganglia. The nervous impulse set up in one branch of the pre-ganglionic fibre passes to the other branches, so to peripheral ganglia, and to tissues more or less remote from

the point stimulated. These reflexes may be called pre-ganglionic axon reflexes. In no case, I think, is a reflex set up in cranial, sacral or sympathetic ganglia by an afferent neuron acting on an efferent neuron. It is impossible at present to say how far these axon reflexes are of importance in the normal working of the body. Whether they occur or not is simply a question of the normal intensity of the mechanical and chemical stimuli affecting the nerve-fibres and nerve-endings. But it cannot, I think, be doubted that in pathological conditions they come into play.

This view of the production of the reflexes was put forward by Anderson and myself. I take it to be the mechanism of (*a*) the reflex secretion of saliva from the sub-maxillary ganglion

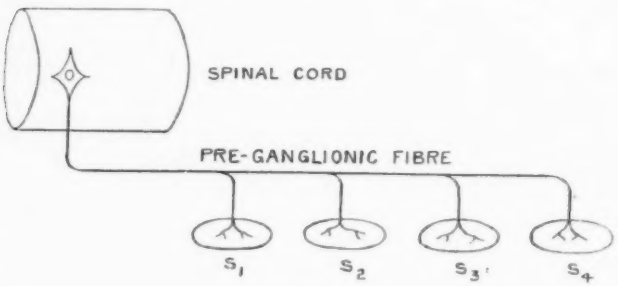

FIG. 4.

Diagram of connection of a nerve-fibre with the ganglia of the lateral sympathetic chain, S_1—S_4, consecutive sympathetic ganglia. The number of ganglia with which the nerve is connected may be greater or less than this.

described by Cl. Bernard, except so far as it is caused by recurrent chorda-tympani fibres; (*b*) of the bladder reflex described by Sokownin; (*c*) the anal and other reflexes by way of the inferior mesenteric ganglia, and the pilo-motor reflexes from the ganglia of the lateral chain described by Anderson and myself; (*d*) the vascular reflexes described by myself.

A few years ago a new peripheral "reflex" was discovered in Pawlow's laboratory by Popielsky, viz., the reflex secretion of pancreatic juice produced by injecting acid into the intestine. This was put forward by Pawlow, Popielsky, Wertheimer, and others, as decisive proof that a true reflex could be given by peripheral ganglia. The view that it was a nervous reflex at all

seemed to me so irreconcilable with the course and distribution of the visceral nerves that I asked Mr. May to investigate the matter. Before, however, he had arrived at any definite proof as to the actual mode of production, Bayliss and Starling who were also investigating the question showed that the secretion was not due to a reflex action, but was due to chemical substances affecting the gland directly.

Distribution of a white ramus as compared with the distribution of its constituent fibres.—It must be noted that in the sympathetic system the pre-ganglionic fibres of any given spinal nerve have a more extensive connection with the peripheral ganglia than any single fibre in it has. As an example I may quote the probable arrangement of the pilo-motor fibres of the first lumbar nerve.

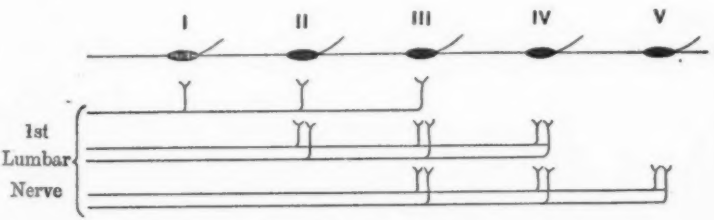

FIG. 5.[1]

Diagram of first lumbar nerve in cat. The nerve sends fibres to five ganglia, the separate fibres usually send branches to three ganglia only; fewer fibres send branches to the first three ganglia than to the subsequent sets of three; the total number of branches received by each ganglion varies, the third lumbar ganglion receives most.

The actual connection of each spinal nerve with the peripheral ganglia I have considered in my article on the "Sympathetic System" in Schäfer's "Text-book of Physiology." It involves too much detail to consider here.

Nerve-cell connections not present in the autonomic system.—I have just said that there is no experimental evidence of a true reflex in sympathetic ganglia, or in the similar ganglia of the cranial and sacral autonomic system. It is, then, experimentally a gratuitous assumption that afferent neurons exist in them. It is also, so far as experiment goes

[1] From *Journ. Physiol.*, XXV., p. 392, 1900.

a gratuitous assumption that a peripheral sympathetic neuron can send an impulse to any other peripheral sympathetic neuron. In a certain number of cases it has been shown, again experimentally, that no such commissural neurons exist. Thus the forms of cell connection shown in fig. 6, may, it appears to me, be excluded from the sympathetic, and probably from the whole autonomic system.

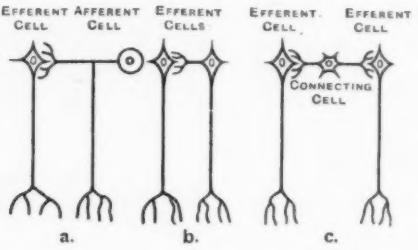

Fig. 6.

Post-ganglionic axon reflexes.—Another form of reflex which I think occurs in the sympathetic system is the post-ganglionic axon reflex, *i.e.*, the spreading out of an impulse from one branch of a peripheral neuron to its other branches. Probably any strong local contraction or irritation brings them into play. Since a neuron, so far as we know, supplies a very limited area of tissue, this reflex must in the first place be very limited in range. But it is capable of extension by the overlapping of the areas of different neurons as in the diagram (fig. 7).

Blocking of impulses in the nerve-cells.—I have been unable to find any evidence that an impulse set up in an autonomic motor nerve-cell can pass back through the cell, and so stimulate adjoining cells in the ganglion. The path backward appears to be blocked in the ganglion cells just as it is in the motor cells of the spinal cord.

There is a part of the autonomic system which I have so far left out of account. This is the *enteric nervous system.* It consists of the neurons of Auerbach's and Meissner's plexuses. There is no clear evidence as to the central

connection of these neurons. The least improbable supposition is, perhaps, that they are connected with vagus fibres in the fore-part of the gut, and with the pelvic nerve-fibres in the hind-part of the gut. But experiments made on rabbits by the nicotine method are not in favour of such connection by the pelvic nerve-fibres. I hope soon to be able to investigate the matter further.

It is from the cells of the enteric nervous system that the best case can be made out for the existence of a peripheral nerve-cell reflex. Bayliss and Starling found that on stimulating a spot of the intestine after all the nerve-fibres to it had been cut, there was contraction above

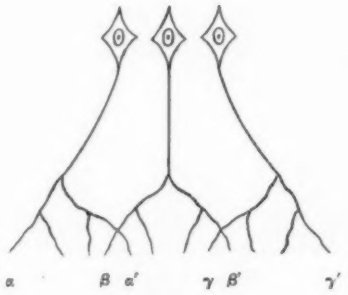

FIG. 7.

Diagram of possible means of spreading from fibre to fibre of post-ganglionic axon reflexes. The impulse set up in α can pass to α'; the contraction brought about here may stimulate β, and thence an impulse can pass to β', and so on.

the spot stimulated, and relaxation below it. Until, however, the nervous connections of these cells are known, the possibility remains that the reflexes may be axon-reflexes.

Comparison of the autonomic system of mammals and other vertebrates.—In the preceding account I have been dealing with the autonomic system in mammals. In its main features the plan I have given holds, I think, for vertebrates generally, and on this I would say a word or two.

In birds the sympathetic vertebral ganglia are more regularly arranged than in mammals, and there is a sympathetic ganglion to each cervical nerve. Moreover, a medullated strand passes between each spinal nerve and its corresponding spinal ganglion. Such a strand in mammals is called a white ramus, and in mammals a white ramus consists chiefly of pre-ganglionic fibres. We might, then, conclude that in birds each spinal nerve sent out pre-ganglionic fibres, in which case the origin of the sympathetic from the spinal cord would not have the local arrangement which it has in mammals. The deduction, however, would be based on a false premiss. In mammals the majority of the post-ganglionic fibres are, it is true, non-medullated, but some are medullated. In birds, and in all other vertebrates except mammals, the majority of the post-ganglionic fibres are medullated, though some are non-medullated.

In birds stimulation of the sympathetic nerves causes sometimes erection, sometimes depression of the feathers, it causes also contraction of the blood-vessels of the skin. These facts afford a basis for investigating the origin, ganglionic connection, and course of the sympathetic fibres. This investigation I have been engaged on, and the results afford good ground for believing that in all essential points the cranial autonomic, the sacral autonomic, and the sympathetic system of birds correspond with that of the mammal.

In reptiles, amphibia and fish, we can compare the anatomical arrangement of the nerve with that existing in birds; and such a comparison seems to me to leave no doubt that in all these the arrangement is fundamentally the same. In fish it is noteworthy that the cranial and sacral autonomic systems are relatively more developed than the sympathetic system.

An interesting point arises from a comparison of the distribution of pre-ganglionic sympathetic fibres in different animals. In the mammal the pre-ganglionic fibres of any one spinal nerve have a wide range of distribution, running it may be to eight or ten vertebral ganglia. And by the

degeneration method I have traced fibres in the lateral sympathetic chain much farther than there is any evidence of their presence by the stimulation method. Moreover the area of distribution varies in different mammals, thus in certain cases it is greater in the dog than in the cat. In birds the area of distribution is also great. In other vertebrates the connections of the pre-ganglionic fibres have not been worked out in detail, but the experiments which have been made on the frog (Waters, Steinach) indicate that the area of distribution is much less. In cartilaginous fish, anatomical observations (Chevrel, Bottazzi) show that the vertebral ganglia are not throughout connected into a longitudinal chain; it appears indeed, that in particular cases the pre-ganglionic fibres of a given spinal nerve run only to the corresponding sympathetic ganglion.

These facts give some basis for supposing that at first the sympathetic system was entirely segmental, the sympathetic pre-ganglionic fibres arising from one segment being connected with one vertebral ganglion only, and that in development the pre-ganglionic fibres have become connected with more and more ganglia of the lateral chain, till we reach the wide distribution which is present in mammals.

Passage of impulses to a tissue from afferent nerve-fibres.—As soon as I deduced, from the state of things in the rabbit and cat brought about by the action of nicotine, that all the nerve-fibres proceeding from the central nervous system have nerve-cells on their course, it followed that no autonomic fibres ran outwards in the somatic branches of the nerves, since no nerve-cells occur on the course of these. Moreover, since I found no autonomic effect on stimulating in the cat the nerve-roots, both anterior and posterior, of a number of nerves—the cervical, certain brachial, lumbar and coccygeal—it followed that these nerves sent no efferent autonomic nerve-fibres to the tissues observed.

These conclusions were in flagrant opposition to the results obtained by Stricker, and by a number of other observers in the presence of vaso-dilator fibres in the posterior roots of the nerves which supply somatic fibres to the hind limb of the dog.

In my article on the "Sympathetic System" in Schäfer's "Text Book of Physiology," I had to face this contradiction in results, and I mentioned there were various ways in which the vascular dilatation could be produced without the presence of efferent vaso-dilator fibres in the posterior roots.

On further consideration of the possible ways, it seemed to me that the vaso-dilator action must be produced by the special sensory apparatus—the spindles—present in muscle, and I expressed the view that they were produced by impulses along these afferent fibres at a time when, so far as I know, everyone who believed in the existence of vascular dilatation, brought about by posterior root-fibres, considered it to be due to efferent fibres. The admirable work of Bayliss has gone a long way to settle the question; he has definitely shown that the impulses pass back by afferent fibres. He does not find that the muscle spindles have any special relation to the vaso-dilator action; he considers that the chief seat of vascular dilation is in the skin; he finds, also, that dilation of the vessels of the intestine can be produced by impulses passing by the afferent fibres of the twelfth and thirteenth thoracic nerves; the evidence for this, however, does not appear to me to be conclusive. It would be out of place in this general statement to enter into a detailed discussion of the subject, and I shall restrict myself to a consideration of some of the broader issues.

The afferent fibres of the special senses we may leave on one side. The nerve-endings of afferent fibres in general must, from the nature of the case, be in contact with the tissue in which they end, but they may be in contact either with formed substance or with the living cells. In nearly all cases, if not in all, the normal stimulus does not pass from tissue to nerve-ending, but is a mechanical or chemical stimulus directly affecting the nerve-endings. There is, then, no obvious reason why the nerve-ending and tissue should be in such intimate connection that a nervous impulse should be able to pass from cell to nerve-ending, or conversely from nerve-ending to cell. Still, if the connection were sufficiently intimate, it is difficult to see why an impulse should not pass from the nerve to the tissue.

If such backward or antidromic action did occur, its effect, if it had any, would be either a chemical change alone, or a chemical change accompanied by contraction or secretion. In specialised endings of the type of Pacinian bodies and touch corpuscles, any change that might be produced would, from the nature of the tissue, be slight and not observable; and the same would probably hold for neuro-tendinous organs.

The obvious cases then in which an observable change might occur are the free nerve-endings in (1) epithelium of the skin; (2) in secretory glands; (3) in cardiac muscle; (4) in unstriated muscle; and (5) in neuro-muscular spindles. With regard to (1) and (2), it is certain that there is no direct evidence of antidromic action, though it may no doubt also be said that further observations are required before it can be asserted that none exists. The depressor is the chief afferent nerve of the heart, and no effect has been observed from stimulating its peripheral end. There is also no accepted instance in which stimulation of afferent fibres in mammals affect any of the viscera largely composed of unstriated muscles, such as the œsophagus, stomach, intestine,[1] bladder, uterus. Nor in the experiments I have made have the unstriated muscles of the hairs been visibly affected by antidromic impulses. In mammals, then, the antidromic action, so far described, is limited to the blood-vessels, and for any certain effect is limited to the blood-vessels of the limbs.

In the limbs we have to consider the blood-vessels of the muscles and deeper lying structures and those of the skin. In the cat I have never seen any flushing of the skin of the foot or stimulation of the posterior roots of lower lumbar or sacral nerves, though pallor of the foot with subsequent flushing is easily produced by stimulating the anterior roots of the upper lumbar nerves or stimulating the sympathetic. In consequence I am not yet convinced that the primary change is not in the muscles. Such change as occurs in the

[1] In the frog contraction of the intestine has been described by Steinach as the result of stimulating the posterior roots. The occurence of this is still a subject of controversy.

skin of the dog might be due to an outspread of change from the muscles. In the muscles, the tissues directly affected by nervous impulses may be the blood-vessels, but I do not think the evidence definitely shows that the blood-vessels are not secondarily affected by changes in the muscle-spindles. And I think we must regard the passage of impulses to a tissue by afferent fibres as occurring only in very special cases. The subject requires further investigation, and it is possible that prolonged excitation of the posterior roots may render obvious effects which now escape observation.

Afferent Fibres.

I pass now to the question of afferent fibres in the autonomic system. The bulbar autonomic, the sacral autonomic and the sympathetic nerves, just peripherally of the posterior root ganglia, all contain afferent fibres, but the peripheral distribution of these has marked points of contrast with that of the afferent fibres, some of which I may mention.

The bulbar and sacral autonomic nerve-trunks apparently send a greater or less number of afferent fibres to all the organs to which they send efferent fibres.

This is not the case with the sympathetic; the sympathetic sends no afferent fibres to the body walls or limbs. It is true that by the degeneration method there is evidence of the presence of one or two afferent fibres in the gray rami, but they apparently end in or close to the vertebral column, and I have not found any reflex on stimulating the gray rami. Moreover, the sympathetic sends no afferent fibres to the head, where its afferent fibres overlap those of the bulbar autonomic, and relatively few (in parts perhaps none) to the region in which it overlaps the sacral autonomic.

The afferent sympathetic fibres overlap the bulbar autonomic fibres in the thoracic viscera, the stomach, intestines, and probably the liver and pancreas. In these regions most of the afferent fibres, which on electrical stimulation give rise to pain, pass by the sympathetic

strands and not by the vagus. It is an old observation on animals that stimulation of the vagus below the diaphragm gives rise to little or no sign of pain. The thoracic and abdominal sympathetic chain, the splanchnic and inferior splanchnic nerves are all markedly sensory. The sympathetic of course sends afferent fibres to viscera such as the kidney, which it alone supplies. It sends also afferent fibres to the mesentery, in the cat, for example, fibres about 8 to 10 μ in diameter, which end in the Pacinian bodies.

Within the region to which the sympathetic system sends afferent fibres there are some points of resemblance between the origin and distribution of efferent and afferent fibres.

The afferent fibres which accompany the sympathetic arise from the nerves which give off efferent fibres, and from these only, *i.e.*, they arise in man from the first thoracic to the second or third lumbar nerves.

The afferent fibres, as the efferent, run in the white rami. By the degeneration method I have obtained evidence that one or two afferent fibres may run in a gray ramus, but I have not been able to obtain any reflex action on stimulation of the central end of a gray ramus.

The distribution of the afferent fibres of the several white rami to the viscera to which they run is, I think, very nearly the same as the distribution of the efferent fibres; it is perhaps a little more extensive. This may be deduced from a comparison the results of Head and others on the referred pain caused by the viscera, with the results of observations on the distribution of the efferent fibres. My own experiments have been made by stimulating the sympathetic chain or its branches, and observing the effect on cutting the rami in succession.

Situation of the cell-bodies of the afferent nerve-fibres.—We may now consider whether the afferent fibres which run with the efferent autonomic fibres have their trophic centre in the spinal or in the peripheral ganglia.

If the blood-vessels of the body wall and limbs, and the unstriated muscle and glands of the skin receive any afferent fibres, these can only have their trophic centre in the

posterior root ganglia, since they do not pass through any ganglion except a posterior root ganglion. And in that case there is no obvious reason why the corresponding structures in the viscera should not also have their trophic centre in the posterior root ganglia.

As regards the white rami, which contain most of the afferent visceral fibres, there is conclusive evidence that the very great majority of them have their trophic centre in the posterior root ganglia. It consists in the fact that after intra-spinal section of a nerve just peripherally of the posterior root ganglia, either all, or all but a few, of the medullated fibres in the white rami degenerate; and that after section of the sympathetic or of the splanchnics or of the inferior splanchnics no degenerated fibres are present in the white rami.

Similarly in the sacral autonomic system, the pelvic nerves contain about 1,000 afferent nerve-fibres, and about twice this number of efferent nerve-fibres; on cutting the roots of the sacral nerve, as was shown by Anderson and myself, about half a dozen fibres only remain undegenerated in the pelvic nerve, and these are probably post-ganglionic medullated fibres.

Of the several thousand afferent medullated fibres then, which run between the spinal cord and the viscera, a dozen or two at most can have their trophic centre in the autonomic ganglia, and there is a reasonable probability that these few remaining fibres are either post-ganglionic medullated fibres or recurrent afferent fibres. And I think it is certain that all the afferent phenomena of the viscera which we are acquainted with must be referred to afferent fibres, the cell-bodies of which are in the posterior root ganglia.

There remains to consider the possibility that there are some afferent fibres which are non-medullated. But these, if they exist, do not give any observable effect on stimulation, for the non-medullated fibres which run with the white rami are simply small gray rami attached to the white ones, and, as I have said, the larger separately-running gray rami produce no observable physiological effect on stimulation of their central ends.

Physiological characteristics of the afferent fibres to the viscera.—If we take the trophic centre of the afferent fibres to the viscera to be the same as that of afferent fibres to other tissues we should naturally suppose that the two sets of afferent fibres would in general produce similar effects. It is, however, well known that there are some striking differences between the afferent nerves to the viscera and the afferent nerves to the skin.

(1) The viscera in a healthy condition give rise to little or no sensation when cut. In pathological conditions, however, cutting may be painful, and strong contraction of the tissue may give rise to intense pain.

(2) The localisation of pain is very imperfect.

(3) In pathological conditions the viscera readily give rise to tenderness and pain in the body wall, that is, to referred pain, a fact which has been dealt with by Ross, Mackenzie, Head, and others, and worked out in detail by Head.

The comparative insensitiveness of the viscera means in physiological language that the "threshold" for sensation is higher in the nerves supplying them than it is in other nerves. This difference in the threshold might be due either to the threshold being higher in the individual nerve-fibres, or to fewer afferent fibres running to a given area. The latter seems to me to be in the main the correct explanation; the number of sensory fibres to the viscera is certainly small in reference to the area they supply. In pathological conditions the receptiveness of the mechanism is increased, and so the threshold is lowered.

There are other possible hypotheses. Thus it is conceivable that on the sensory side, as on the motor, an additional cell is introduced on the course of the impulses, and that an additional cell should raise the threshold for sensation. If such a cell were present in the spinal ganglion it must, in view of the fact that the fibres on the two sides of the ganglion are equal in number, be of the type shown in the fig. 8. This possibility seems to me most unlikely, but, unfortunately, it is not easy to see how to disprove it experimentally.

It is usually supposed that referred pain is due to visceral

fibres or their collaterals becoming connected with the nerve-cells in the cord which receive impulses from the somatic fibres. In such case the upward path to the brain would, in fact, travel by somatic tracts and be referred to the distribution of the somatic nerves. It is worth notice that if the autonomic tissues of the body wall have afferent fibres, there may be two kinds of referred pain, one affecting the autonomic nerves of the body wall, the other the somatic nerves.

A view has recently been put forward by Dr. Mackenzie that the afferent fibres of the viscera cannot give rise to anything but referred pain. Regarded subjectively it is certain that pain arising in the viscera is recognised as such. If Dr. Mackenzie's view is right, it follows that when we refer

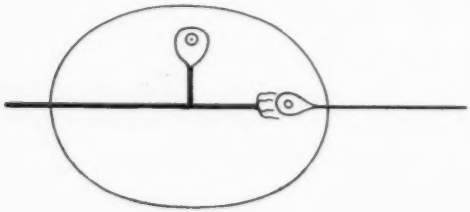

FIG. 8.

pain to the viscera, though the cause of it is there, it is an error of judgment on our part, it ought to be felt in the body wall.

The difficulty in the way of this view is that we can localise pain in the skin and in the body muscles, so that if visceral pain were solely in the skin or muscles, we ought always to feel it in the skin or muscles.

The only way out of this difficulty seems to me to suppose that certain kinds of pain in muscle we have learnt to associate with disorders in the viscera, so that whenever these particular kinds of pain are felt, we refer them to the viscera. Although this explanation is possible, it is, I think, excessively unlikely.

In what I have said so far I have dealt with what seem to me facts about the afferent fibres accompanying the efferent autonomic nerves, but I have put on one side the fundamental difficulty with regard to them, and that is: Are there any afferent nerves which deserve to be separated from afferent somatic nerves, and if so, what are the characteristics of autonomic as opposed to somatic afferent nerves? I have above tried to show that the afferent nerves of the sympathetic system are indistinguishable in form and position from those of the somatic system, and it remains to consider what other distinguishing characters may be present.

On the efferent side the somatic fibres are those which run to striated muscle; all other efferent fibres are autonomic.

It is clear that we cannot make a like division of afferent fibres according as they run to striated muscles or to other tissue; it would lead to nothing but confusion to consider the afferent fibres of the skin as autonomic fibres and the afferent fibres of striated muscle as the only somatic afferent fibres.

We might, however, restrict the afferent autonomic fibres to those which end in tissues which receive efferent autonomic fibres, *i.e.*, in mammals to the afferent fibres of unstriated muscle, cardiac muscle, and glands, and in some other vertebrates probably some connective tissue cells also. But we know little or nothing with regard to any special connection of afferent fibres with these tissues, and it is quite possible that they have none which are not essentially similar to afferent fibres elsewhere. If this classification were adopted, it is to be noted that the trunks of the efferent autonomic nerves would be accompanied by afferent somatic nerves, for they contain fibres which have no special connection with these autonomic tissues; in the sympathetic of the cat, for example, there are the nerve-fibres of the Pacinian bodies.

Leaving on one side the nerves of the special senses, all that seems to me possible at present towards arranging afferent fibres into autonomic and somatic divisions is to consider as afferent autonomic fibres those which give rise

to reflexes in autonomic tissues, and which are incapable of directly giving rise to sensation; and to consider all other afferent fibres as somatic. On this basis it follows (1) that the afferent fibres accompanying the efferent autonomic are in part somatic, since the vagus, the pelvic nerve, and every white ramus of the sympathetic can give rise to pain; (2) that afferent autonomic fibres are present in all spinal and most cranial nerves; and on the view I have given above as to the position of the trophic centre of the afferent fibres, it follows also (3) that all the posterior root ganglia contain autonomic as well as somatic nerve-cells.

Since the efferent autonomic fibres are all small nerve-fibres, it naturally suggested itself that the afferent autonomic fibres might be distinguished from the afferent somatic fibres by their size. This, however, is not the case. Nerve-fibres capable of giving rise to sensation are of all sizes; fibres giving rise to direct reflexes in autonomic tissues are, it is true, chiefly small, but there is some evidence that they may be as large as 10μ.

Since by hypothesis the one kind of fibre gives rise to sensation, and the other does not, there must be a difference in their central connection, such that in the one the upward path to the cerebral hemispheres is absent or very slightly developed. That, and that only, so far as we can say, distinguishes autonomic from somatic afferent fibres. Further progress waits for the discovery of some distinguishing histological character. And in the meantime it is open to discussion whether the class of afferent fibres which are solely reflex in function can be properly considered as corresponding on the afferent side to the efferent fibres of the autonomic tissues.

AN ACCOUNT OF THE NERVE-CELLS IN THIRTY-THREE CASES OF INSANITY, WITH SPECIAL REFERENCE TO THOSE OF THE SPINAL GANGLIA.

BY JOHN TURNER, M.B.ABER.

I PROPOSE to give an account of the spinal ganglia cells in a series of cases of insanity, and of the larger nerve-cells of the cortex and spinal cord.

I have restricted myself to the larger cells of the central nervous system as I do not believe we are yet in a position to speak of changes affecting the chromatoplasm of the smaller with any degree of certainty.

Of late years, since the introduction of the Nissl method, a considerable amount of attention has been bestowed on the posterior root ganglia, at first chiefly in relation to their connection with tabes and later with relation to general paralysis, and a large amount of experimental work has been done in the study of the effects of various poisons and injuries on their cells.

In a valuable contribution on the relationship of changes in the spinal ganglia cells to general paralysis which appeared in vol. xxiv. of BRAIN, 1901, Orr and Rows[1] give a fairly complete list of the recent literature on the subject up to that date, and also a very useful synopsis of the views held by the chief authorities as to the normal varieties of cells met with in these ganglia in different animals, and they give five cell types met with in the human ganglia, based upon Lugaro's description of the five types he has found in dogs.

I will briefly recapitulate those given by Orr and Rows.

(1) A cell corresponding to Lugaro's first type in dogs. Large and clear (which I take to mean a cell whose

chromatoplasm stains sharply with no colouration of the ground substance). The granules are sparse and towards the periphery increase in size and form a more or less defined dark ring, outside this again is a colourless zone devoid of granules. These cells are the most numerous.

(2) A cell corresponding to Lugaro's second type in dogs, distinguished from the preceding by the large size of the peripheral chromophilic elements arranged as a definite ring near the periphery. These stand next to the previous in point of numbers.

They describe a perinuclear space as existing in both these types.

(3) A cell corresponding to Lugaro's darkly-stained variety in dogs, of which Orr and Rows describe two varieties, a large and a small. In the latter the chromophilic elements are very minute, with indistinct outline, and are scattered diffusely throughout the cytoplasm. In the former the chromophilic elements are larger and are arranged in two concentric systems, one around the nucleus and the other towards the periphery. In both the ground substance (spongioplasm) stains deeply and more or less obscures the chromophilic elements. The nucleus is central, the perinuclear space not well seen and the outer clear zone narrow.

(4) Two varieties, in both of which the chromophilic elements are large and sparsely scattered, the ground substance is unstained or very lightly coloured, the nucleus central, and the perinuclear space and outer clear zone are prominent features :—

(*a*) A small variety in which the chromophilic elements are smaller and arranged concentrically around the nucleus.

(*β*) A medium-sized variety in which the chromophilic elements are large and not so concentrically arranged.

(5) A cell of medium size corresponding to Lugaro's fifth type in the dog, and which both he and they term, on account of the peculiar whorl-like arrangement of the chromophilic elements, a vorticose cell.

After a careful inspection of my cases I am not able to convince myself of the existence of all these types as distinct entities. I am not able to draw a distinction between their

types one and two; all grades are met with insensibly blending from the one to the other, consequently I have grouped these two together. And as regards the dark cells I look upon the large variety described by Orr and Rows as pathological; or at all events the only dark cells of the large variety which I have seen appear to me to be abnormal, inasmuch as they vary extraordinarily in the frequency with which they occur; and the outer clear zone is absent, and the nucleus presents more or less a darkly-stained and dense appearance.

In the small variety of dark cells I find the nucleus very often eccentric, and as in cats and puppies it is also very commonly so situated, I am inclined to regard it as a normal condition.

As the vorticose cell is only met with very occasionally, I have for practical purpose disregarded it in my classification, which consists of the following divisions:—(1) Large cells, corresponding to Orr and Rows' types 1 and 2; (2) Medium-sized cells, corresponding to their type 4 B.; (3) Small cells, corresponding to their small variety, type 3.

At an early period in my investigations I came across masses of ten or twelve large cells in certain ganglia, apparently fused together, and without evidence of any capsule separating one from another. These cells stained somewhat darkly, and contained very small, dark, homogeneous nuclei without any perinuclear space. Subsequently I met with a similar appearance in the spinal ganglia of a puppy. This raised doubts as to whether such a condition was pathological or due rather to injury during removal. To test this point I purposely injured some of the ganglia in a young adult cat by compressing them with forceps. The injured cells could readily be detected in sections; they were distorted and often forced more or less completely from their capsule; they stained deeply and their nucleus was small, often eliptical, dark and homogeneous. Fused cell masses were also seen, having the general characteristics of those formerly met with. Uninjured cells, or, at all events, cells presenting a normal appearance, occurred amongst injured cells. In another trial very slight pressure, indeed, served to set up all

these changes in the ganglia cells of a puppy 23 days old. This fairly conclusively shows that these large masses of cells are artefacts, but it does not apply to the cases where two or three normal-looking cells are in apposition, a condition often met with, and which will be discussed later on.

The effect of the injury, both on the cytoplasm in causing it to stain deeper, and especially on the nucleus, is very interesting. The nucleus presents an appearance identical to that described first by Sarbo as homogeneous degeneration. Very often the external cells in a ganglion, removed with every care, show these changes in the nucleus, rather pointing to the fact that very slight damage to the cell is sufficient to alter its characters.

Both in the injured and uninjured ganglia certain cells were met with which had a great affinity for erythrosin and did not retain the toluidin blue, so that they appeared as more or less homogeneous red masses and resembled cells found at times among my cases, especially in one of tabes.

Method employed.—The ganglia were fixed for 20 to 24 hours in saturated solution of sublimate and then passed through graded alcohols, chloroform, and finally embedded in paraffin. The sections were fixed to the slide by Gulland's method and stained generally with erythrosin and toluidin blue. Other stains used were Vessale's hæmatoxylin and Benda's iron-hæmatoxylin; this latter is admirable for the cells of cats, kittens, and puppies, but is not so suitable for detecting pathological changes as toluidin blue and erythrosin.

The method of fixation employed, as shown by the animal's ganglia, produces very slight shrinking of the cells; they fit closely their capsules. Sometimes with human cells the shrinking is very considerable, but I think that this is due to some tissue condition present in life—some chemical change resulting in a more fluid state of the protoplasm. Very generally in sections which show these shrunken cells, others occur in their vicinity which do not show any appreciable shrinking.

The spinal cord was examined for tract degenerations by the following method, which I have found gives very satis-

factory results :—After prolonged hardening in Muller's fluid —two months and upwards—small pieces are placed in 2 per cent. osmic acid solution to which sufficient carbolic acid has been added to give a deep straw colour (2 or 3 drops of 90 per cent. or a corresponding amount of a 5 per cent. solution). They are left in this in the dark for 36 to 48 hours, and if the pieces are occasionally moved about quite thick pieces ($\frac{3}{16}$ inch) will be thoroughly impregnated by the osmic acid in this time. They are then rinsed in water, passed through alcohol (24 hours), chloroform (2 hours), paraffin, and cut. It is advisable to give two changes of both alcohol and chloroform.

II.

The following is a brief account of each case :

No. 1.—C. W., a female, aged 42, died of phthisis pulmonalis in an advanced stage of general paralysis. Autopsy held three and a quarter hours after death. Five ganglia examined.

Large cells—average size 80 by 80 μ—large space between cell and capsule. The outer clear zone is broad in some but generally consists of an irregular, ragged-looking area ; the nucleus is central, clear, with no perinuclear space in most cases, very narrow in others. Some excess of pale yellow pigment. A considerable number of the large cells are shrunken, distorted and darkly stained.

Small cells, average 36 by 36 μ. They are more or less rounded or angular. The outer clear zone is replaced by threads running from cell to capsule. The nucleus often peripheral, no perinuclear space, some pigment.

There is patchy over-growth of connective tissue in places and proliferation of the capsular cells which often replace nerve-cells, filling up the space that they formerly occupied. No engorgment of blood-vessels or excess of leucocytes.

Remarks.—Probably the most general abnormal appearance is the circumferential chromatolysis with central nucleus. The proliferation of connective tissue and capsule cells although decided is much less than is often met with in general paralysis.

No. 2.—A. M., male, aged 36. Chronic mania. In robust health, died of choking. Autopsy twenty-one hours after death. Five ganglia examined.

Large cells show all grades of staining, from the usual clear granular appearance to very dense with all detail obscured, and

these latter are usually very shrunken and distorted. The average size is about 80 by 50 μ, and there is greater separation from the capsule than in the previous case. The outer clear zone is represented by a shreddy structure which is often wide and irregular. The nucleus is central; in the healthy-looking cells it is plump (15 to 18 μ) and clear, in other cases it is darkly stained and small (9 to 10 μ). Frequently, but not always, this kind of nucleus is seen in the darkly-stained cells and usually around them only is a perinuclear space visible. Excess of golden pigment seen.

Small cells show nothing to call for notice, except that they contain a considerable quantity of dark (green with toluidin blue) pigment.

The connective tissue and capsular cell proliferation is quite as marked as in the previous case. Very considerable engorgement of the vessels, most marked in the cervical ganglia, no increase of leucocytes.

Cortex.—The Betz cells of the paracentral convolution* are dark, due to staining of ground substance, but the Nissl-bodies are well defined. Their nucleus is peripheral in a few instances.

Cord.—In the cervical enlargement and mid-dorsal, the fore-horn cells and those of Clarke's column appear normal. In the lumbar enlargement the cells stain diffusely and deeply, and the Nissl-bodies are obscure.

The cord was examined for tract degeneration, but gave a negative result.

Remarks.—The changes noted in the ganglia are the same as in Case 1, viz., peripheral chromatolysis, and dark staining of some of the large cells, more than in the previous case.

No. 3.—M. A. W., a female, aged 47 years. Chronic melancholia, she died of pericarditis. Autopsy three hours after death. Four ganglia examined.

The large cells show very little shrinking from capsule, but many are in a state of peripheral chromatolysis with a very broad, irregular, web-like outer zone, so that in some cases the chromatoplasm occupies quite a small area, but still around its edge can often be seen the ring of large, dark flakes. The nucleus is central and appears normal, and there is usually a narrow perinuclear space. The pigment is in small amount and with erythrosin shows brightly-stained red particles amongst it.

* The sections of brain in all cases were taken at right angles to the median longitudinal fissure passing through the top of the ascending frontal and paracentral convolutions.

The small cells present the usual appearance and a peripheral nucleus is a frequent occurrence. They contain a considerable quantity of pigment (green with toluidin blue.) A few vorticose cells are seen.

There is considerable overgrowth of connective tissue in places, with proliferation of the capsular cells, which latter sometimes quite block up the capsular space. Blood-vessels are not a prominent feature and there is no excess of leucocytes in them.

Cortex.—The Betz cells contain an excess of pigment, but their chromatoplasm shows a fairly normal appearance. In the frontal region chromatolysis of the larger pyramids with peripheral nucleus was a common feature. The fore-horn cells of the cervical, dorsal and lumbar regions, beyond excess of pigment in the latter, and some shrinking and dark staining in the former, call for no remark.

No. 4.—A. L., a female, aged 17 years. Admitted in a state of acute delirious mania supervening on a previously depressed state. She died of pneumonia after six weeks' residence. Autopsy six hours after death. Four ganglia examined.

Large cells.—A considerable number show axonal reaction. In one cervical ganglion there was a patch of dark, shrunken cells with homogeneous nucleus and no perinuclear space. The average size of the large cells is smaller than usual (66 μ).

Middle-sized cells have a very pale centre with no chromophilic elements, a peripheral nucleus and a dark outer rim of flakes. The small cells call for no remark, and there was no special alteration of the connective tissue noted nor venous engorgement.

Cortex.—The Betz cells and larger pyramids in the paracentral convolution were in an advanced state of axonal reaction, and beside this they stained very deeply, whereas as a rule they are pale when in this condition.

Medulla and cord.—The cells stained densely. A few in the cervical and dorsal region showed the axonal reaction, only one or two in the lumbar. The cells of Clarke's column were markedly affected. Transverse sections of the cervical cord gave a negative result for tract degeneration, but in longitudinal section a few scattered fibres gave the Marchi reaction in the pyramidal tracts and direct cerebellar; none in the posterior columns. Longitudinal sections of the dorsal cord showed considerably more degeneration in the pyramidal tracts (Marchi reaction) and very slight in the posterior columns. In the lumbar region a similar condition prevailed and about to the

same extent as in the dorsal. There was very little pigment, (which stained brown) in the forehorn cells.

Remarks.—The tract degenerations in this case may be compared with those met with in Nos. 7, 28 and 31, which were also cases characterised by axonal reaction cells.

No. 5.—F. C., a female general paralytic, aged 29 years. Autopsy twenty-one hours after death. Eight ganglia examined.

Large cells.—A great number were darkly stained, shrunken and distorted, the peripheral clear zone absent or represented by a few shreds stretching to the capsule. Nucleus dark and homogeneously stained and frequently very small, in some cases peripheral, a perinuclear space is often not visible, occasionally it is very wide. Practically no pigment.

Small cells.—Nucleus often peripheral. A considerable amount of pigment (dark green with Toluidin blue) is present, chiefly deposited around the nucleus. Several instances of two cells in apposition, chiefly among the small cells. A continuous dark line runs down between the opposed parts (fig. 10). In the clear nuclei of the large cells dark curved or S-shaped bands occur occasionally. These are about 2 μ thick at the centre and taper at the ends.

There was no increase of connective tissue or capsular cells noted. The perigangliar sinuses were engorged, and contained large numbers of polynuclear leucocytes.

There was considerable degeneration, both old and recent, in the crossed pyramidal tracts, most marked in the cervical region.

Remarks.—Large masses of cells apparently fused together were met with in some of the ganglia; these were probably caused by injury during removal, and we must bear in mind the possibility of the small, dark nuclei observed being due to the same cause.

The dark lines noted in some of the nuclei I am inclined to look upon as similar to those observed by Roncoroni in the nuclei of cortical nerve-cells. He believes they are linin structures, but as to their significance we know nothing; they are not, however, as Lugaro imagined, artificially produced by a shrinking or pleating of the nuclear capsule, caused by the alcohol used in the preparation of the specimens, as I have been able * to show them in cells prepared by my film method, where no alcohol or any other shrinking agent is used.

No. 6.—H. E., female, aged 40 years, suffering from agitated melancholia, died of pneumonia. Autopsy.—Head examined

* See *Journal of Pathology and Bacteriology*, vol. vii., Dec. 1900.

six hours after death; cord twenty-seven, only one ganglion examined (thoracic).

Large cells. Generally oval or round, and with very little shrinking from capsule, they average 80 to 100 μ. The greater number have a well-marked clear outer zone, and a more or less clearly defined ring of chromophilic flakes internal to it. There is in general a fine crumbling of the chromatoplasm, giving the cell an uniform pale colour; whilst occasionally all the central chromatoplasm is absent, and nothing but the peripheral ring remains. The nucleus has generally a normal appearance and is central. About a quarter of the number of large cells are deeply stained and slightly distorted, and their nucleus is smaller and denser and sometimes puckered, with a wide perinuclear space, which is not seen in cells with normal nuclei. Very little pigment.

Middle-sized cells show marked central chromatolysis with a pale washed-out appearance.

Small cells generally dark and heavily pigmented, the pigment staining dark green with Toluidin blue, and usually clustered around the nucleus. Some of the small cells are pale, with a well-defined outer ring of chromatoplasm; these do not contain pigment.

The blood-vessels are somewhat engorged, and there was a slight proliferation of connective tissue in places.

Cortex.—Practically all the Betz cells and larger pyramids are in a state of axonal reaction.

Cord.—The forehorn cells at the cervical enlargement, beyond the fact that one or two are in a state of axonal reaction call for no remark. At the lumbar enlargement rather more instances of axonal reaction are met with, and all the cells in the region corresponding to Clarke's column are in this condition.

Remarks.—The condition of central chromatolysis noted in so many of the spinal ganglia cells in this case probably correspond to one of the changes which Fleming [3] noted in animals' spinal ganglia cells after severance of the peripheral nerves.

No. 7.—M. L., female, aged 42 years, with a history of previous depression and rapid onset of dementia. Stated to have been a very sober woman; was only an inmate for five weeks. Autopsy held twenty-six hours after death; no obvious cause for this was discovered beyond the changes noted microscopically. Only one (thoracic) ganglion examined. Many of the cells from this ganglion were in a condition of axonal reaction, some in the form associated with peripheral nucleus, others in that with central nucleus and chromatolysis of the middle region of the cell (see previous case).

The larger cortical cells of the paracentral convolution all presented the same condition. The fore-horn cells of the cervical, mid-dorsal and lumbar levels were fairly normal, but Clarke's column cells were affected.

There were slight degenerative changes in both the pyramidal tract and posterior columns in the cervical and mid-dorsal levels, but the lumbar cord (transverse section only examined) gave a negative result.

No. 8.—F. C., female, aged 41 years, suffering from agitated melancholia. She developed parotitis and died with symptoms of a septicæmic nature. Her temperature was below normal till the day of her death, when it shot up to 104° F. Autopsy held twenty-two hours after. Four ganglia examined.

The condition which was found affecting all the cells in these ganglia was that known as acute cell change or coagulation necrosis. With toluidin blue and erythrosin they stained of a rather pale homogeneous purple, sometimes with a continuous (not broken up into flakes) dark outer rim but never showing any clear peripheral zone. A characteristic feature of spinal ganglia cells in this condition is the absence of any ragged edge. They have a smooth outline formed by the dark ring mentioned. Sometimes, indeed often, they appear to be peppered over with very minute blue grains on a rosy back-ground. No trace of a perinuclear space can be seen, and the nucleus is central and often denser than usual, although slightly paler than the cytoplasm with which it almost insensibly blends. The axis cylinder stains more deeply than usual and is much thinner than usual (see fig. 8). The cells are generally somewhat distorted and shrunken from the capsule.

The connective tissue was scanty and there was no proliferation of capsular cells.

There was some engorgement of blood vessels with excess of leucocytes chiefly polynuclear.

A similar form of cell change was found in the paracentral convolution, and in a modified form in the hypoglossal nucleus and cervical fore-horn cells, but not in the dorsal.

No. 9.—A. W., female, general paralytic, aged 21 years. Autopsy four hours after death. Only one ganglion examined.

The cells are all uniformly small, darkly stained and irregular in outline, and have no clear outer zone and no distinct chromophilic granules. The largest is only 45 μ. The nucleus is small, central homogeneously stained, and with slight or no perinuclear space. Only a small amount of pigment noted in any of the cells.

The main feature is the marked proliferation of the capsular cells; each capsule consists of several layers of cells instead of one.

No. 10.—M. F., a weak-minded woman, with chronic melancholia, who died, much emaciated, of pneumonia, aged 49 years. Autopsy twenty-four hours after death. Three ganglia examined.

Large cells generally pale and with chromatolysis of central region and central nucleus, which is usually small and dark and homogeneous, and with a very wide perinuculear space which does not appear empty but contains a pale reticulum. Scattered among the pale cells are many darkly-stained and distorted specimens in which the outer clear zone is absent or represented by a few spoke-like threads. In these cells the perinuclear space is absent, or very small, and they contain a considerable amount of yellow pigment (*cf.* left-hand cell of fig. 9).

Many of the small cells are very irregular in outline and have multilocular appearance and much pigment. The nucleus is often peripheral.

There is very marked engorgement of vessels, but no increase of leucocytes.

The cells of the paracentral convolution were in a condition of axonal reaction. The hypoglossal cells were normal, but those of the cuneate and gracile nuclei showed the axonal change. The cells of Clarke's column were all in this condition, but in both the cervical and lumbar regions only an occasional specimen was seen among the forehorn cells.

There was very slight degeneration (Marchi reaction) in longitudinal section of the crossed pyramidal tracts in the cervical and dorsal regions, but practically none in the lumbar. This condition was much more marked in the dorsal region.

Remarks.—Many of the cells in the ganglia are in a condition of axonal reaction (*vide* Cases 6 and 7).

A prominent feature is the very general alteration in the nuclei. The relation they may have to *post-mortem* changes must be borne in mind, but it may be pointed out that although this alteration is very common yet it co-exists with normal nuclei, and not unfrequently the two kinds occur in neighbouring cells.

No. 11.—A. O., a male, aged 34 years, died in status epilepticus, and at the autopsy nine and a half hours after death a gliomatous tumour of the right frontal region the size of a tangerine orange was found. His other organs were healthy. Eight ganglia examined.

Large cells.—A very general condition of dark staining met with, with absence of outer clear zone and more or less distortion

and shrinking. Considerable quantity of yellow pigment. The nucleus is central and is very often darkly stained and homogeneous, small, but not puckered. No indication of any perinuclear space even around the smallest nuclei, except in one or two instances. The outer ring of chromatoplasm often appears as a continuous band. One or two instances of extremely advanced chromatolysis met with where only a small patch of chromatoplasm remained, all the rest of the cell body having a nearly colourless, ground-glass looking appearance (*cf.* fig. 3).

Medium-sized cells similar to the large.

Small cells call for no remark.

There is considerable proliferation of the capsular cells, and in many instances the capsules are quite filled up with them. Sometimes small clumps of very darkly-stained nuclei are met with, representing a more chronic condition of the above. Also there are many instances of invasion of the pericellular space by nuclei, probably wandering leucocytes.

Considerable engorgement of the blood-vessels, but very few leucocytes noted.

The paracentral cells had a fairly well marked stichochrome appearance. but there was some staining of the ground substance. Nucleus normal. A few instances of axonal reaction noted.

In the cervical enlargement the forehorn cells were shrunken, but had a fairly normal stichochrome appearance with central nucleus. In the lumbar enlargement the cells were similar, but not so shrunken.

His cord was examined, but beyond slight Marchi reaction in the crossed pyramidal tract, more marked in the cervical region and on one side, gave no signs of degenerative changes.

No. 12.—A. M. C., a female general paralytic, aged 23 years, died of acute colitis and peritonitis. Autopsy twenty-four hours after death. Six ganglia examined; some of them (especially the thoracic) were much smaller than usual.

Large cells, especially in the larger ganglia, appear fairly healthy; some, however, are darkly stained, irregular in outline, and loculated. A peripheral chromatolysis is fairly general. Only a small amount of pigment. The nucleus is central, and very rarely darkly-coloured or homogeneous; the perinuclear space is very narrow or absent.

Many of the medium-sized and small cells are dark and loculated, especially in the small ganglia.

There is considerable proliferation of the capsular cells, and many small clumps of darkly-stained nuclei representing the sites of former nerve-cells.

No engorgement of blood-vessels, and only very few leucocytes seen.

No. 13.—E. B. E., a female, aged 32 years, who died after a few days' residence in a state of acute delirious mania. Her temperature from admission was as follows: November 6, 1901, E. = 104°; November 7, M. = 103°, E. = 103°; November 8, M. = 101°, E. = 103·2°; November 9, M. = 100·6°, E. = 102·4°; November 10, M. = 101·4°, E. = 102°. The autopsy was held twenty-eight and a half hours after death, and seven ganglia were examined. All these and the pericellular spaces and vessels of the cord were crowded by a micro-organism having the morphological appearance of the bacillus of malignant œdema. The cells of the ganglia were all in the condition of acute cell change, and contained a large quantity of yellow pigment (fig. 7). As a rule they were somewhat more darkly-stained than usual in this condition (compare figs. 7 and 8).

No connective tissue changes or proliferation of capsular cells noted.

Blood-vessels engorged, but showed very few leucocytes.

The cells of the paracentral convolution and the cord were all in the condition of acute cell-change. The cord was examined for tract degeneration, but gave a negative result.

No. 14.—E. P., a female, aged 28 years, suffering from chronic mania, died of typhoid fever. Autopsy five hours after death. Three ganglia examined. The following is her temperature for four days prior to death.

May 5, M. = 103° F., E. = 105°; May 6, M. = 105·4 falling to 103° after sponging, E. = 105·4 falling to 102·8° after sponging; May 7, M. = 104·4°, E. = 105·4°; May 8, at 7 a.m. 105·6°, at 9 a.m. 106°, died at 9.20 a.m.

The large cells are generally rounded and with very little pigment, and fit their capsule closely. Quite a half of them stain darkly and show no outer clear zone, but have generally a dark rim. A peripheral nucleus is common; in fact, the prevailing and predominant type of change is one of axonal reaction, some with chromatolysis and peripheral nucleus, others with central chromatolysis and central nucleus; in some cases only the outer rim of chromatoplasm remains, and the space between this and the nucleus is quite pale and devoid of granules. Probably the cells are in a very early stage of acute cell change as well, but those which do not show the axonal reaction often present a fairly normal arrangement of their chromatoplasm (see fig. 1). The nucleus is often darkly and homogeneously stained, and shows

dark lines within it at times (*vide* case 5); there is no perinuclear space. The nucleolus is frequently pale, loculated and swollen (7 to 8 μ).

The middle-sized and small cells are in the majority of instances in a condition of axonal reaction.

There is a slight increase of connective tissue, and some venous engorgement, but no increase of leucocytes. The walls of the arteries are very markedly thickened, apparently due to increase of middle coat.

The cells of the paracentral convolutions are in a typical state of acute cell-change. The fore-horn cells of the cervical enlargement contain definite Nissl-granules, but they are less distinct than normal, whilst in the lumbar enlargement these bodies are still less distinct, and the ground substance was stained.

The spinal cord was examined for Marchi reaction, and showed very slight degeneration in the posterior columns only.

Remarks.—Beyond the condition of axonal reaction noted, it is probable that the spinal ganglia cells have begun to take on the acute cell change, as shown by the general faint staining and the blue colouration of the axis cylinders close to their origin. This, however, is open to question. This was one of the few cases where a temperature of 106° F. was reached; we should expect, on the ground that a mere pyrexial condition is responsible for this change, to find the cells unmistakably showing it, whereas they are so slightly affected that one can only recognise the alteration by at best somewhat equivocal signs.

This case should be compared with No. 13, where with a much slighter rise of temperature the change was unquestionable.

No. 15.—S. M., female, aged 45 years, suffered from agitated melancholia on a weak-minded basis, and died of pneumonia. Autopsy five hours after death. Only two ganglia examined; a cystic condition of one noted.

The large cells showed much distortion and shrinking with frequent absence of the outer clear zone. Large amount of yellow pigment present. Only a few stained darkly. The nucleus was central, small, darkly and homogeneously stained with a very wide perinuclear space as a rule. The small cells were also pigmented. Considerable venous engorgement with excess of leucocytes chiefly polynuclear.

No marked changes in the connective tissue or capsular cells.

The cells of the paracentral convolution were in a state of axonal reaction.

The spinal cord was examined for Marchi reaction and showed very slight degeneration in the lumbar region only; both the crossed pyramidal tract and posterior columns very affected, and also the posterior roots at their entry into the cord.

No. 16.—W. B., aged 14 years. A male idiot, died of cerebral hæmorrhage. Only one ganglion examined.

The large cells are generally rounded or oval, but are smaller than usual, the largest not more than 60 μ in diameter. The outer clear zone is absent, but the outer rim of large flakes is present. The nucleus is central and has generally a normal appearance, no perinuclear space. Very little pigment seen in any of the cells.

The small cells and connective tissue call for no remark.

No. 17.—O. M. D., female, aged 19 years. Epileptic imbecile, died asphyxiated during a fit. A well-nourished girl, with healthy organs. Autopsy held five hours after death. Eight ganglia examined.

Large cells stained distinctly and clearly and all of much the same intensity, presenting a granular appearance with well-defined border of larger flakes. The outer clear zone is narrow, and in many is not seen at all. No marked shrinking of cell. The axis cylinders are stout, and do not stain in the vicinity of their cell of origin. The nucleus is central, in some ganglia the majority of them have a normal appearance, in others a considerable number are more or less darkly and homogeneously stained, in these latter the nucleolus is commonly swollen and pale, measures sometimes 8 μ. As a rule no perinuclear space is visible. Very little pigment.

Middle-sized cells have coarsely granular contents and somewhat peripheral nucleus.

Small cells appear normal. In several instances two or even three are in apposition.

There is considerable proliferation of the capsular cells, so that not uncommonly the nerve-cell is surrounded by two or more layers of them.

No engorgement of blood-vessels or increase of leucocytes.

The Betz cells of the cortex have shrunken dendrites, the ground substance is stained and the Nissl-bodies indistinct; the nucleus is central. The large pyramids show central chromatolysis with central position of nucleus. The fore-horn cells of the cord stain densely, but the Nissl-bodies are distinct; both cells and processes are shrunken. The nucleus is central.

Remarks. Although in these ganglia there was no very

marked evidence of cytoplasmic changes, the nucleus was very frequently altered in character and showed homogeneous degeneration. The probabilities that this was a *post-mortem* change are greatly negatived by the fact that the autopsy was held only five hours after death in cool weather.

No. 18.—H. J. S., male, aged 43 years. A case of acute mania; died of bronchitis. Autopsy held ten hours after death. Eight ganglia examined.

Large cells.—There are a considerable number of shrunken dark-stained cells, in many cases heavily pigmented. These have no clear peripheral zone, but are bordered by the rim of dark flakes which tend to fuse together. They show chromophilic granules on a dark background in the area within the outer dark rim. The nucleus is dense but not manifestly reduced in size (see cell to left in fig. 9). The majority of the large cells, however, are not markedly shrunken, they have an outer clear zone which varies in width and appearance, in some it is nearly an homogeneous structure, in others a delicate network. Internal to this, even when it is very wide, is an extremely well-marked ring of coarse flakes (see right-hand cell of fig. 9). The nucleus is central and in the majority of cases darkly and homogeneously stained. It is diminished in size, and, indeed, in some cases is scarcely larger than the nucleolus. There is a wide perinuclear space varying in width inversely to the size of the nucleus, it has sometimes a loosely reticular appearance, and at others shows a collection of pale granules around the nucleus with a clear space between them and the border of the cytoplasm. A few vacuolated cells are seen (very common in cats, kittens, and puppies). Occasionally a cell consists entirely of a very pale blue structureless material (hyaline degeneration). The small cells have very little or no pigment, they present the usual appearance and have very commonly a peripheral nucleus.

The middle-sized cells generally contain a dark homogeneous nucleus.

Localised patches of small round cell proliferation occur, the nuclei (3 to 4 μ) being smaller than those of the capsular cells. They probably represent leucocyte infiltration.

There is marked engorgement of the blood-vessels and large numbers of polynuclear leucocytes.

The cells of the paracentral lobe and the fore-horn cells of the cervical and dorsal regions of the cord showed a fairly normal stichochrome appearance. Those in the lumbar region were darkly stained and shrunken, and their Nissl-granules somewhat

obscured in consequence. Examination of both longitudinal and transverse sections of the cord for tract degeneration gave an entirely negative result.

No. 19.—A. N. M., female, aged 37 years. Congenitally deficient to a slight extent, kept to her bed for nearly seven years before coming here, and was said to be hypochondriacal, emotional, spiteful, and with an uncontrollable temper. During her residence here for five months was simple, silly and lazy, but gave no trouble. Died of colitis. Autopsy held seventeen hours after death. Seven ganglia examined.

Large (and medium-sized) cells.—About a third of the number are dark and distorted, and many show nuclei attached to them (leucocytes). They appear in all stages of destruction, loculated and vacuolated, others are pale and in a state of axonal reaction. A considerable amount of yellow pigment is present. Very seldom is any perinuclear space discernible. Some of the ganglia show fewer cells in the state of axonal reaction than others. In these former the cells generally have a more healthy appearance. The axis cylinders, at their point of origin, stain light blue with toluidin blue.

The small cells call for no remark.

There is a considerable increase of connective tissue, and many little clumps of dark nuclei are met with, representing the sites of former nerve-cells. No marked proliferation of capsular cells.

Some venous engorgment, but no increase of leucocytes. Masses of fibrin threads enclosing, in some cases, leucocytes, seen in some of the periganglionic vessels. In the paracentral convolutions the majority of the large cells are in an early state of axonal reaction. The forehorn cells of cervical, dorsal, and lumbar regions appear fairly healthy.

After hardening in Müller's fluid the cord showed distinctly pallor, limited to Goll's column in the cervical region, and in the upper dorsal a more diffuse pallor of the major part of both posterior columns. This passing downwards got progressively less, and at the upper lumbar region was no longer discernible.

In osmic acid preparations, in both posterior columns (Goll and Burdach's) of cervical, dorsal and lumbar regions, there was an extremely marked degeneration characterised by Marchi reaction. It was most marked in the cervical and dorsal regions, but still very considerable in the lumbar. The column of Goll was much more affected than that of Burdach. No degeneration was noted in any other tracts. The posterior nerve-roots in the lumbar and cervical regions were degenerated and gave a plentiful Marchi reaction.

Remarks.—A noticeable feature in these ganglia is the evidence they show of cell destruction, active and passive. Probably many of the dark ones are already functionless and practically dead, and the invading nuclei are in process of removing them. With this state of affairs is associated degeneration of the posterior columns, chiefly that of Goll, and also degeneration of the posterior nerve-roots. And the amount of degeneration as shown by the Marchi reaction is very considerable.

This woman, while resident here, was not confined to bed till shortly before her death, and nothing special was noted in regard to her gait. On admission her knee jerks were exaggerated and her plantar reflexes brisk and of the flexor type; unfortunately there is no note of their condition later on.

No. 20.—R. R., a male general paralytic, aged 35 years, died of colitis. Autopsy twenty-two hours after death. Seven ganglia examined.

Large cells. In some ganglia nearly half the number are darkly stained and with small dark nucleus. In others only a few are seen. Not much pigment as a rule. The nucleus is often slightly puckered and central, a dark homogeneous staining of it is common in some ganglia, this form is especially associated with the large dark cells. The perinuclear space is very narrow or absent.

The small cells call for no remark except that two or three in apposition are occasionally seen (fig. 11).

There is considerable engorgement of the vessels and a fair number of polynuclear leucocytes.

No marked changes in either the connective tissue or capsular cells.

No. 21.—B. H., a male imbecile, died of capillary bronchitis, aged 13 years. Autopsy thirty-six hours after death. Six ganglia examined.

The cells all stain of much the same depth, appearing granular on a clear ground. The outer clear zone is rarely to be seen. No perinuclear space. Very little pigment in any of the types of cell. The nucleus is central, except very occasionally.

Practically no dark homogeneous nuclei are met with, but they often appear slightly denser than usual. Dark S-shaped and straight lines noted.

The cells are sparsely scattered except at the edges of the ganglia. No vascular engorgement, and no connective tissue or capsular overgrowth.

The cells of the paracentral lobe look as though they were in the

early stage of acute cell change, but many stain darkly, obscuring their detail. The forehorn cells of the cord also stain deeply. In both cortex and cord cells were occasionally seen of a light blue hyaline appearance.

Remarks.—Although the autopsy was not held till thirty-six hours after death, the nuclei of the spinal ganglia cells do not stain darkly and homogeneously.

No. 22.—E. J., a female general paralytic, aged 44 years. Autopsy held twenty-two hours after death. Six ganglia examined.

Only a few healthy-looking cells seen; the commonest changes are absence of outer clear zone, which is replaced by a frayed-out border, great distortion and marked peripheral chromatolysis, only the peripheral rim of flakes which takes the form of a continuous band being retained. In fact, a considerable number of the larger cells show the central nucleus form of axonal reaction.

Pigment in fairly large amount is present; often deposited as a sharply defined greenish (with toluidin blue) mass around the nucleus, which latter is in many cases dark and homogeneous and peripheral. The nucleolus is sometimes large (7 μ), at others small (4 μ) and pale. No perinuclear canal to be seen. There are many very darkly stained cells.

Masses of fibrin threads seen in the vessels, or long single threads staining (with erythrosin) bright crimson. Many polynuclear leucocytes.

The increase of connective tissue and capsular cells is inconsiderable. In the periganglionic tissue, however, there was very marked increase of round cells.

No. 23.—R. W., a female, general paralytic, aged 31 years. Autopsy eleven hours after death. Eight ganglia examined. All showed the same general characters, marked overgrowth of capsular cells, lying two or three deep around the nerve-cells, overgrowth of connective tissue, exudation of round cells about the vessels.

Large cells.—Some fit their capsules closely, others are much shrunken and loculated. Probably more than half are darkly stained and distorted with a frayed-out edge. The nucleus is generally small, dark and homogeneous, and central; the perinuclear space very wide and containing granules. A considerable amount of pigment is present, more especially in the dark cells. A clear outer zone is generally present in the pale.

The small cells are heavily pigmented.

Some engorgement of vessels, but no leucocytes noted.

Many clumps of dark nuclei seen, representing sites of former nerve-cells.

No. 24.—S. D., a female with symptoms resembling an acute case of general paralysis, aged 34 years. Her temperature for the last three days was as follows:—M. 103·4, E. 106·6; M. 101·8, E. 103 2; M. 104·8, E. 106·4. No obvious cause of death was discovered at the autopsy held twenty hours after. Seven ganglia were examined, one contained a small cyst.

The condition of all was similar, they showed the acute cell change, superimposed on a previous condition of axonal reaction. But only a large proportion and not all the cells were in the latter condition.

There was some engorgement of blood-vessels, but no excess of leucocytes. No marked connective tissue or capsular changes.

The cells of the paracentral convolution and the cervical and lumbar fore-horn showed acute cell change, and in the two former regions the axonal reaction was clearly marked as well, but not in the latter.

Remarks.—This woman was stated to have had an alcoholic history. Unfortunately her cord was mislaid, and no osmic acid preparations were made.

No. 25.—R. B., female, aged 18, an imbecile and epileptic. She died from meningeal hæmorrhage. The autopsy was held thirty-two hours after death. Six ganglia were examined.

In all sections a large majority of the cells appear shrunken, and the attenuated axis cylinder can sometimes be detected passing across the wide pericellular space; but in all sections also some cells of each type fit their capsule closely, indicating that the fixation is not at fault, but that a more fluid condition of the cell protoplasm obtains in some cases, which, after dehydration, necessarily results in shrinking.

The main feature with all types is that they stain rose colour with erythrosin, and do not retain the toluidin blue; the nucleus appears as a homogeneous rosy body not readily differentiated from the cytoplasm. No perinuclear space. The nucleolus is almost colourless; there is no outer clear zone. Conjoined cells are met with.

The connective tissue is increased in places, and there is some proliferation of the capsular cells.

No engorgement of vessels.

The cells of the paracentral convolution all stain lightly. The ground substance is coloured, and there are very few Nissl-bodies.

The cells are small and their processes few and thin. The nucleus is small and homogeneous, and sometimes has a clear area around it. It is frequently peripheral. No pigment noted. They seem few in number. The fore-horn cells of the cord have the usual stichochrome appearance, but their nuclei are often small and homogeneous.

No. 26.—I. L., a female, aged 64 years; she suffered from chronic melancholia, with much agitation, and died of pneumonia. Autopsy twelve hours after death. Eight ganglia examined.

The majority of the cells, large and small, are shrunken and distorted, but a few fit their capsule closely. There is excess of yellow pigment. In sections stained for some little time in erythrosin and then in toluidin blue the nucleolus stains pale red with a darker border, and the nucleus red and somewhat homogeneous, small and crenated. Roughly speaking, the more shrivelled the nucleus the larger the perinuclear space is. Side by side can be seen cells with small solid red nuclei only 8 μ in diameter, and others with large normal nuclei 18 μ in diameter, and with barely any perinuclear space. The cells generally seem to be in various stages of decay, and some are mere misshapen red or hyaline masses, with no chromatoplasm.

The connective tissue is considerably increased, and contains a copious deposit of fine-grained pigment (green, with toluidin blue). In the paracentral convolution some of the Betz cells appear normal, others are darkly stained and shrunken, with a very small nucleus, denser than normal, and often peripherally situated. There are large deposits of yellow pigment in the cells. The pyramidal cells are shrunken, and their nucleus dark and homogeneous. The fore-horn cells of the cervical enlargement appear normal.

In osmic acid preparations of the cord in the cervical region, longitudinal sections, showed a Marchi reaction affecting scattered fibres of the posterior column. A slighter amount of degeneration was noted in the crossed pyramidal tracts. In the mid-dorsal region there was very slight degeneration in the posterior columns and none elsewhere. The lumbar cord gave a negative result.

No. 27.—A. B., female, aged 57 years, admitted in a feeble and demented condition, unable to walk; died after three weeks' residence. For the last eight days her temperature varied between 99° F. and 102·6°. Autopsy fourteen hours after death. Four or five ganglia examined.

The cells generally appeared to be in an early condition of the acute cell change. They showed no outer clear zone, and were

much distorted and shrunken. The whole cell body stained uniformly, showing very fine, blue grains, and no outer ring of chromatoplasm. There was no perinuclear space, and the nucleus was frequently of much the same density as the cytoplasm, and not clearly demarcated therefrom. In some instances it appeared normal. Large clumps of yellow pigment were in most of the large cells. A few cells were dark and with small homogeneous nuclei; a few appeared in the condition of axonal reaction. The axis cylinders of the more affected cells were attenuated, but did not stain deeply in the immediate neighbourhood of the cell.

There was considerable engorgement of the vessels, and large numbers of polynuclear leucocytes.

No marked connective tissue or capsular changes.

The Betz cells and large pyramids of the paracentral convolutions showed a normal stichochrome appearance, but the former contained a large quantity of yellow pigment. The cortical arterioles were thickened and tortuous and some had ruptured. Collections of fibrin threads were noted in some of the vessels.

In the cervical enlargement the fore-horn cells stained very densely, but still contained Nissl-bodies somewhat obscured owing to the general dark colour of the cell. The nucleus was central and dense. A similar condition was found in the lumbar enlargement, except that here the nuclei were clear.

Transverse sections of the dorsal and lumbar regions of the cord and longitudinal sections of the former as well were examined for tract degeneration, but gave a negative result. Transverse sections of a posterior peripheral nerve at its junction with a posterior spinal ganglion showed a perfectly normal appearance.

Remarks.—The uniform staining and very fine state of the Nissl-granules, together with the dense nucleus indistinctly marked off from the cell body, the absence of the clear outer zone and peripheral ring of chromatoplasm and the attenuated axis cylinder point strongly to these cells being in an early stage of acute cell change. This was not corroborated by the condition of the cerebral and spinal cord cells. The absence, however, of the change in these latter regions does not necessarily negative the supposition, but points rather to a greater susceptibility of the ganglion cells, in this case to the specific cause of the morbid condition, or else to a greater localisation of the cause, supposing it to be a toxine in these parts.

No. 28.—H. R., a female, aged 35 years. Admitted in a state of acute mania stated to be due to "severe influenza." In course of time she lapsed into a demented condition and died,

without any very obvious cause for death discovered at the autopsy. Her stomach was completely filled with pieces of sheeting, blanket, and hair. Autopsy twenty-two hours after death. Seven or eight ganglia examined.

The majority of the cells of all the types are in various stages of axonal reaction, and quite a large number appear as perfectly colourless hyaline masses, probably representing an extreme degree of the change. Both the central and peripheral nucleus type is met with (figs. 4 and 5). The less affected cells stain pale, and have a uniform fine powdering of their chromatoplasm. Some are shrunken and darkly stained. The nucleus is often small and puckered, or else very small, with smooth outline, homogeneous, and taking on the erythrosin stain. No signs of a perinuclear space in most cases.

There is a fair amount of pigment sometimes arranged around the nucleus in the form of a crescent, which appears of a yellow or dull green colour, and is in some cases studded with bright red granules (erythrosin).

Vacuolated cells are common, some are filled with small vacuoles. Conjoined cells in twos and threes noted.

A very marked increase of the connective tissue in some ganglia and many little round clumps of dark nuclei.

The vessels are engorged and often packed with polynuclear leucocytes.

The larger cells and Betz cells of the paracentral convolutions are in a state of axonal reaction. The cervical fore-horn cells did not show this change, nor was there any appearance of it in the Purkinje cells.

Transverse sections of the cord showed slight pallor in the column of Goll and paucity of nerve-fibres, with corresponding increase of connective tissue. There was no other evidence of tract degeneration discovered. Cross sections of two of the peripheral nerves adjoining the ganglia also appeared quite healthy.

Remarks.—If the two specimens of sensory nerves examined may be taken as representative of these nerves in general, it is somewhat surprising that they showed no evidence of degeneration, considering the large number of spinal ganglia cells which were affected. Experiments have shown that it is precisely sections of these peripheral nerves which sets up a change in the ganglia cells, whilst sections of the posterior roots between the ganglia and the cord does not affect them (2). Possibly there may have been degenerative changes at more distal points.

No. 29.—M. A. W., a female, aged 53 years, admitted in a feeble and stuporose state. She died in a fortnight's time. A tumour (? glioma) the size of a Tangerine orange was found in the left frontal region of the brain. Her temperature, which had been uniformly low, shot up to 105·6° F. on the day of her death. Autopsy held twenty-three hours after. Nine ganglia examined, of which three were in a state of cystic degeneration, and one was almost entirely destroyed by the cyst. The cells in these three were extremely distorted and shrunken, with a smooth contour. They stained uniformly red, and the nucleus blended with the cytoplasm, and was nearly the same colour. Its position was central. Many cells were largely occupied by a yellow pigment, and some entirely. The cells in the other ganglia appeared to be in an early stage of acute cell change. They were all much the same colour, pale and powdered over with fine blue granules, and there was no peripheral rim of larger flakes. They were shrunken and their borders frayed out. The nucleus was central, homogeneous, but not as a rule very dark, although slightly darker than the cytoplasm. Generally there was no visible perinuclear space, occasionally a very narrow one could be detected. The axis cylinders of the more affected cells were attenuated, but only very lightly stained; of the less affected they were of average calibre.

There was some proliferation of the capsular cells and venous engorgement with large numbers of polynuclear leucocytes, and intravascular deposition of fibrin in the cystic ganglia, but no marked changes in the others.

The cells of the paracentral convolution, cerebellum, pons and cord all showed acute cell change, but those in the lumbar forehorn showed less marked change than those in the cervical region, and in the former situation many retained a fair number of Nissl-bodies, although their ground substance was uniformly stained. And a similar condition characterised the cells of the hypoglossal nucleus.

The cord was examined and showed in the cervical region very marked recent degeneration, chiefly limited to Burdach's column. The posterior roots appeared unaffected. In the dorsal region there was somewhat less marked degeneration of Burdach's column and chiefly on one side. In the lumbar region the degeneration of Burdach's column was slight, but the posterior roots at their entry to the cord, and the anterior roots both within and just without the cord, showed the Marchi reaction. There were no signs of degeneration in any of the other tracts. One of

the cystic ganglia was examined for Marchi reaction with a negative result.

Remarks.—Probably the degeneration noted in this case was due to the cystic destruction of ganglia. Other cases of acute cell change (13, 27, 31) failed to show any degeneration in the cord.

No. 30.—H. W., a male, aged 46 years, a house painter, admitted in an anæmic condition with a blue line on his gums and apparently unable to walk. At first he was delirious for a few days, but a month after admission he was noted to be quiet and placid, with slurred and tremulous speech, taking but little interest in his surrouudings ; and so he remained until the morning of his death, when he had a "seizure," was convulsed, and lost consciousness. The autopsy was held six hours after death and 8 ganglia examined.

The majority of the cells are pale and the Nissl-granules fine and powdery and evenly distributed over the cytoplasm with no peripheral rim of larger flakes. A few of the middle-sized cells show fairly large and discrete granules. A great many of the pale cells fit their capsule closely, but the darkly-stained, distorted ones (which have a great affinity for erythrosin) have a wide pericellular space. Many also show extreme chromatolysis, consisting of a large colourless mass with a little patch of Nissl-granules at one side in which the nucleus lies. This latter is very small, homogeneous, and red, and shows no perinucleur space (fig. 3). Such cells are swollen and often contain a large vacuole.

The above description applies chiefly to the thoracic ganglia, in the dorsal and lumbar the cells are apparently more affected. The majority being distorted, shrunken, some staining dark red, others pale red, with a small, dark peripheral nucleus, sometimes half protruding from the cell. These latter have an hyaline appearance. Not much pigment seen in any of the cells.

No marked alteration in the connective tissue or capsular cells and no vascular changes.

Sections from the paracentral convolution of both sides were similar, they stained badly with none of the usual sharpness in the cell details. The cells of all the layers were shrunken, especially the dendrites of the larger pyramidal and Betz cells. The majority, including these last, stained deeply with colouring of the ground substance, which obscured the Nissl-bodies. In some of the paler there is a general crumbling of these, except quite at the periphery. A vorticose arrangement of the attenuated Nissl-bodies in cells is quite common. At a short distance from the body, the apex appears colourless, owing to

disappearance of the chromatoplasm. The Betz cells contain a very large amount of yellow pigment. The very dark ones show no internal detail, their nucleus is small and quite at the side. Batches of very shrunken and very darkly-stained pyramids occur in amongst groups of quite pale cells.

Nucleus.—More often than otherwise it is peripheral, or it may even project from the cell; it is dense, varying in colour from an uniform gray to a dark blue, sometimes of a distinctly reddish tinge, although only stained with toluidin blue. Shrinking is associated with density, the very small are very dense. It is often elliptical, and in this case lies with its long diameter across the cell. Occasionally it is surrounded by a thick rim of chromatoplasm.

Vascular changes.—There is some thickening of the walls of the arterioles of the cortex. Many vessels have their lumen filled with a pale blue structureless mass, and the smaller ones are commonly ruptured.

The cells of the hypoglossal nucleus, and of the cord, presented the usual stichochrome appearance.

Examination of the cord for tract degeneration showed a paucity of fibres and increase of connective tissue in the crossed pyramidal tracts, but practically no Marchi reaction here. This condition was marked in all three of the regions examined (cervical, dorsal and lumbar). The posterior columns showed increase of connective tissue and a considerable amount of recent degeneration (Marchi reaction), most marked in the cervical region, and chiefly in the posterior part of the columns, near the periphery of the cord. The lumbar fore-horn cells contained a quantity of pigment which had stained black.

Remarks.—I have quoted this case at some length as it presents several points of interest. Unfortunately I did not know of the association of lead till after the autopsy and no peripheral nerves were examined. He had symptoms suggesting general paralysis, but there were no macroscopical appearances at the autopsy, nor, subsequently, microscopical, to support this diagnosis. The condition of extreme chromatolysis observed in some of the ganglia cells corresponds to Flemings'[3] description of one form of change produced by severing the peripheral sensory nerves. Pallor of the cells and fine powdering of the chromatoplasm was observed by both Lugaro[2] and Nissl[2] in the ganglia cells of dogs after lead poisoning, but as will have been noticed in other cases mentioned previously it is in no wise peculiar to lead, it appears as an early stage in acute cell change.

With reference to the cortical changes, Schäffer[2] after chronic lead poisoning in dogs and rabbits found two forms of degeneration: (1) a fine granular degeneration, and (2) a homogeneous caused by a fusing of the chromatoplasm with the ground substance. Nissl[3] found in the cortex after lead poisoning a dissolution of the body of the cell and destruction of the nucleus, which was more deeply stained, and its membrane and the nucleolus both disappear. In every case there was eventually a dissolution (paling and disappearance of the Nissl-bodies) of the cells, so that at last only an ill-defined, pale-blue, shadowy form remained. It will be seen that the changes I found in the cortical cells do not strikingly harmonise with either Schäffer's or Nissl's findings, but they may not in my case have been directly or mainly due to lead. The most striking and constant change which I found was the homogeneous degeneration of the nucleus which apparently was also observed by Nissl.

The association of the seizure with the occurrence of the small cortical hæmorrhages and the hyaline masses in the vessels are points worthy of attention. Halliburton[4] and Mott[5] have suggested that the seizures of general paralysis may be due to intravascular clotting resulting in venous stasis, and they have demonstrated that a nucleo-proteid which can be obtained in small quantities from the cerebro-spinal fluid in these cases will cause clotting if injected in the blood stream of an animal.

In view of the appearances seen in this case, it would seem as though we might not unreasonably apply the above theory here, and regard the seizure as the result of blocking of the small cortical vessels and their subsequent rupture. The obstruction being caused by intravascular clotting of nucleo-proteid origin.

These hyaline intravascular bodies—spheres or large irregular masses—are very frequently seen in the cortex in insanity especially in cases of general paralysis.

No. 31.—F. M., a female, aged 40 years, suffered from acute delirious mania and died of pneumonia. The autopsy was held thirty-six hours after death. Her temperature was very irregular and never above 100° F. for the five days preceding death, whilst at times during this period it was sub-normal. Six ganglia were examined.

The cells generally were in a state of acute cell change. They were shrunken and distorted, with smooth contour; the Nissl-granules were absent or existed as a fine powder with sometimes a dark thin outer rim. The nucleus was generally central, more or less homogeneous and allied to the cytoplasm in

appearance. Perinuclear space quite invisible. The cells had a great affinity for erythrosin. The axis cylinders were thin and stained red quite up to the cell. The nucleolus was very pale and of a reddish tinge.

There was some increase of connective tissue and many little clumps of dark nuclei, representing the sites of former ganglion cells, were seen. No vascular changes.

The Betz cells were darkly stained, and all detail in them was consequently obscured. The nucleus was dense and generally central. The cervical fore-horn cells were shrunken and somewhat darkly stained, but the Nissl-granules were distinct. The lumbar fore-horn cells were heavily pigmented and their Nissl-granules not so distinct.

Examination of the cord for tract degeneration gave a negative result.

Remarks.—The cortical cells were in the condition which I have previously noted as occurring in some cases of acute delirious mania.*

No. 32.—S. W., a female, aged 29 years, died shortly after admission from acute alcoholic insanity with peripheral neuritis. Her temperature while here was uniformly subnormal. Autopsy held eleven hours after death, six ganglia examined.

The chief change noted is one of axonal reaction. The cells generally are pale, but here and there a dark one is met with. They are not shrunken and contain very little pigment. There is some powdering of the Nissl-granules and frequent absence of the peripheral rim of flakes. The nucleus is often situated eccentrically, and is plump and with an open mesh work appearance and no perinuclear space. In some ganglia they are denser and tend to stain red. They are often swollen (22 μ) or even ruptured. The nucleolus is pale.

The small cells are heavily pigmented.

There is marked proliferation of the capsular cells and numerous clumps of small dark nuclei representing the sites of former ganglion cells. The connective tissue is not manifestly increased. There is some venous engorgement with large numbers of polynuclear leucocytes. Intravascular collections of fibrin threads which stain bright red with erythrosin are noted, and in some cases the fibrin appears to be outside the vessel as well. The Betz cells of both paracentral convolutions are in a state of axonal reaction. There is excess of polynuclear leucocytes in the vessels of the cortex. The cells of Purkinje,

* *Brit. Med. Journal*, Sept. 22, 1900.

of the hypoglossal, nucleus, and of the cervical fore-horn were not affected, but those of the cuneate nucleus of the dorsal and lumbar fore-horn and Clarke's column were.

Examination of the cord for tract degeneration gave the following results: Cervical regions.—Transverse and longitudinal sections showed slight recent degeneration principally in the columns of Goll and Burdach and scattered irregularly throughout them. The posterior nerve-roots at their entrance into the cord were not markedly affected. The crossed pyramidal tracts were very slightly affected. Mid-dorsal region.—A similar condition was found but more marked. Lumbar region.—There was very marked reaction in the posterior roots at their entrance into the cord and also in both Goll and Burdach column. The degeneration in the crossed pyramidal tract was also more marked. Transverse section of nerves close to the distal side of the ganglia in two instances appeared normal. The only peripheral nerve examined was the posterior tibial and transverse sections of this showed very marked changes. In every bundle only a few myelin rings remained.

Remarks.—The character of the changes found in this case points to the longer duration of those affecting the lumbar fore-horn cells and their axons as shown by the lesions in the posterior tibial nerve. The presence of the Marchi reaction in the posterior roots, posterior columns and crossed pyramidal tracts, in like manner indicate a more recent affection of these fibres and their cells of origin.

This woman had been a heavy drinker for years but her insanity was of short duration and acute. These clinical observations are in accord with the pathological deductions.

No. 33.—A. P., a male, aged 49 years, with locomotor ataxia and a Charcot's knee. His symptoms were those of general paralysis, but unfortunately only sections from one paracentral convolution were examined, and these did not present any signs of this disease. The autopsy was held ten hours after death and six ganglia were examined.

The dorsal and lumbar ganglia were much more affected than the cervical. Their cells, when stained with erythrosin and toluidin blue, retain none of the latter, but appear of a pale, yellowish red with a darker border, and often contain a mass of yellow pigment. They are distorted and shrunken. The nucleus (central) can barely be discerned, appearing as a slightly paler halo around a granular and nearly colourless nucleolus. There is enormous increase of connective tissue and capsular

cells. Many of the ganglia cells are beset with small round nuclei which stain blue, and are about 6 μ in diameter. Sometimes as many as ten can be counted about one ganglion cell.

Some of the cervical ganglia show a considerable number of cells similar to those just described, others few or none. The more healthy specimens retain their Nissl-granules and the peripheral ring of flakes is generally seen. The outer clear zone is not often present. The nucleus is central and only in a few cases shows homogeneous degeneration. There is no perinuclear space. Pallor and swelling (6 μ) of nucleolus is common.

There is little, if any, overgrowth of connective tissue noted in the less-affected ganglia.

Sections of the cord showed marked pallor of the posterior columns visible to the naked eye, and most evident in the lower part. It affected both Burdach's and Goll's column. The myelinated fibres were notably diminished in numbers, with a corresponding increase of connective tissue. Longitudinal sections of the lumbar region across the posterior columns showed also this condition, both in the cord and the posterior roots, but gave no evidence of recent degeneration.

Remarks.—The great reduction in numbers of the nerve-fibres in posterior roots and posterior columns favours the assumption that the altered ganglia cells here found were practically dead cells.

For convenience of reference I append the following table, giving a rough estimation of the recent degeneration (Marchi reaction) noted in the crossed pyramidal tracts and posterior column of the cord. Except in Nos. 5, 19, 31 and 32 it was not of a very marked nature, but even where only one + is used half-a-dozen degenerated fibres could be seen in the low-power field (× 100) of a longitudinal section. Where a minus sign is used it indicates that the examination gave a negative result; where the space is left blank no examination was made. In two of the cases (Nos. 28 and 32) only old-standing degeneration was noted in the posterior columns. In No. 5 both old-standing and recent were combined. In Nos. 15 and 31 the posterior roots in the lumbar region only, gave a decided Marchi reaction and in No. 19 both cervical and lumbar posterior roots were affected. In several instances there was slight degeneration noted in the direct cerebellar tract.

Number of Case.	Cervical Region.		Dorsal Region.		Lumbar Region.	
	Crossed Pyramidal Tracts.	Posterior Columns.	Crossed Pyramidal Tracts.	Posterior Columns.	Crossed Pyramidal Tracts.	Posterior Columns.
2	—	—	—	—	—	—
4	+	—	++	—	++	—
5	+++	—	++	—	++	—
7	++	+	++	++	—	—
10	+		+		—	
11	++	—	+	—	+	—
12	++	—	+	—	+	—
13	—	—	—	—	—	—
14	—	+	—	+	—	+
15	—	—			+	+
18	—	—	—	—	—	—
19	—	+++++	—	++++	—	++++
26	+	++	—	+	—	—
27			—	—	—	—
28	—	Old deg.	—	Old deg.	—	Old deg.
29	—	++++	—	+++	—	+
30	—	+++	—	++	—	++
31	—	—	—	—	—	—
32	—	+	++	+++	++	+++
33	—	Old deg.	—	Old deg.	—	Old deg.

Only five of the cases examined failed to show some degenerative change in the cord. Ten showed it in the posterior columns, and nine in the crossed pyramidal tracts.

These results are satisfactory as they show that changes in the ganglia cells are associated with changes in their efferent fibres, and as it has been shown that severance of the posterior roots does not affect the ganglia cells, we may look upon the changes observed in them as the cause of the degeneration noticed in the posterior roots and posterior columns.

Nos. 13, 27 and 31, all cases of acute cell change showed no tract degeneration, probably because they died before such became evident. It would seem from the observations of Head and Campbell[7] that some days (ten) must elapse before affections of the ganglia cells set up degeneration in their efferent fibres. No. 29 showed very marked degeneration in the column of Burdach on both sides in the cervical region, and on one side in the dorsal. This was a case of acute cell change, but several of the ganglia were in a state of cystic degeneration and one was nearly destroyed thereby.

III.

Under this section I propose to discuss some of the more obvious changes seen in the posterior ganglia and the cortex, in the following order:—(1) Acute cell change; (2) axonal reaction; (3) peripheral chromatolysis with central nucleus; (4) dark-staining of posterior ganglia cells; (5) nuclear changes; (6) fused or conjoined cells; (7) changes affecting the supporting tissue and blood-vessels of the posterior ganglia.

Acute Cell Change.

Synonyms: coagulation necrosis—pyrexial change.

This condition occurred in the posterior ganglia in six of my cases (Nos. 8, 13, 24, 27, 29 and 31) and practically affected all the cells of the ganglia examined; it was associated in all but Nos. 24 and 27 with a similar condition of the cortical cells. I am strongly of opinion having regard to the class of cases in which it occurs that it is due to the action of some poison.

Halliburton's[4] and Mott's[5] experiments have shown that a temperature of 108° F. will produce it even in brains after death, and they have pointed out that this temperature coincides with the coagulation under certain conditions (prolonged heating) of one of the three cell proteids, and from these investigations they conclude that this change is purely the result of proteid coagulation caused by a temperature of 108° F., and Halliburton definitely asserts that such a temperature is *necessary* to produce this change.

No one would deny in the face of such evidence that a temperature of 108° F. can produce this condition, and probably in the manner they suggest, but that it is the sole, or indeed, the usual cause of the change, I cannot admit.

It is obviously ridiculous to attempt to explain on this ground the appearance of the cells in any of the six cases under consideration, because in not a single instance was such a temperature attained. In 1898 I published in Brain an account of this change occurring in the cortical cells in

ten cases of insanity, in not one of which also was a temperature of 108° F. reached. In most of these the maximum reached was 103° F., and in one there was practically no rise of temperature at all.

Perhaps the most conclusive piece of evidence showing the subsidiary position that temperature takes in the production of this change, and which also, I think, is strongly suggestive of its toxic character, occurred in the case of a male general paralytic, whose brain I examined; this man had purulent meningitis, but his temperature never exceeded 101·8° F. From the region of the paracentral convolution I have sections, over one half of which there is purulent effusion beneath the meninges. Now the cells which lie beneath the affected membranes present a typical appearance of acute cell change, whilst those which lie in the farther end of the section removed from the purulent exudate do not. Some of them show probably commencing alteration, but the farther away from the diseased membrane they lie the healthier they are, until quite at the opposite end they show the usual stichochrome appearance, and present a vivid contrast to the cells at the other end of the section which do not retain a trace of Nissl-bodies.

Is it not probable that some toxic substances can bring about a coagulation of the cell proteids as well as heat? Such a conception would allow us to utilise Halliburton's and Mott's valuable suggestions as to the essential cause of the change whether the temperature reaches 108° or not.

The incidence of the change affords another reason, if such is needed, against temperature alone being the essential cause of the alteration. In Case 8 the cells of the paracentral lobe are affected; the cells of the hypoglossal nuclei show indications of change, but at the mid-dorsal level of the cord there are no signs of it. In Case 13 the change implicated the paracentral and the cord cells at all three levels examined, and in the lumbar region they were thickly beset with micro-organisms similar to those seen in the root ganglia. This woman it will be noticed for four days prior to death had a temperature ranging between 100·6 and 103·2. Contrast this case with No. 16 where with a tem-

perature between 105° and 106° for nearly forty-eight hours previous to death the change was barely perceptible in the root ganglia (fig. 1), although well marked in the paracentral cells, and slightly in the cervical and lumbar enlargements.

Cases 6 and 25 are interesting, inasmuch as they show the super-position of an acute change on cells already affected by a more chronic one. They undoubtedly present appearances pointing to acute cell change, but the very marked peripheral position of the nucleus, &c., indicates a previous state of axonal reaction. In the first of these cases the paracentral cells were in the axonal condition, while the fore-horn cells of the cervical region showed it in a very slight degree, and those of the lumbar region more markedly. In the latter case the paracentral and cervical fore-horn cells showed axonal reaction. The lumbar cells did not, but these and the cervical were in the acute cell state. In Case 28 the change was practically confined to the root ganglia, and in Case 30, while these cells only showed early acute change (not marked), those of the paracentral convolution on both sides and the Purkinje cells showed well-marked changes. The cells of the hypoglossal nuclei and cervical fore-horn were slightly affected, and those of the lumbar enlargement even less.

It may be suggested that the reason why the change affects cells in certain regions and leaves others unaffected, is due to a greater susceptibility of those affected, but against this supposition is the fact that the order in which the cells are affected is not always the same; in some cases the spinal ganglia are chiefly implicated, in others the cortical or cord cells, and although usually when the cortex is affected and some of the spinal cells, the cervical are more often affected than the lumbar, yet occasionally (see Case 14) the reverse is the case.

Axonal Reaction.

First known as reaction *à distance*. The term axonal reaction was introduced by Adolf Meyer. I use it merely as a short and convenient designation, and with no reference

to any supposititious causal connection between axon and cell change. It occurs frequently in the posterior ganglia cells (see Nos. 4, 6, 7, 10, 14, 19, 22, 24, 28, 30, 32), but, unlike the acute cell change, it never in any of my cases affected all the cells, although in some cases (notably Nos. 14, 19, 28, 30, and 32) a very large number showed the change. In all but three of the cases (Nos. 14, 22, and 30) a similar condition of the cortical cells occurs, while Case 15 showed axonal reaction in the cortex, but not in the posterior ganglia.

It can be produced by severance of the axis cylinders, and also apparently by cutting off the stimuli from cells which normally pass to or influence others (Warrington, Van Gehuchten). The first of these methods is beyond a doubt. Lugaro[10] has recently questioned the second. A third view has also been brought forward which postulates a direct action on the cell of certain toxines, *e.g.*, pellagrous poisoning, phosphorus poisoning, tetanus poisoning, typhoid poisoning, and alcohol. This last view is also open to question, inasmuch as most of the deleterious agents mentioned certainly set up peripheral neuritis, and perhaps all, and until it is definitely determined that the peripheral nerves or the distal ending of central nerves do not suffer under these conditions, it remains a debatable point whether the alterations in the cells are not secondary to the peripheral changes. Dr. S. J. Cole[6] in a recent paper to this journal has vigorously advocated the directly poisonous action of alcohol on the nerve-cells as a cause of this change. The most serious objection that he urges against the reaction at a distance theory is that in cases of central neuritis, *e.g.*, in cases where the Betz cells are attacked, together with their extensions in the pyramidal tracts, the degeneration in these is quite insignificant compared to the amount of cell change. If this be true it constitutes a grave, if not insuperable, difficulty to the axonal theory, but, judging from my own cases, I am not prepared at present to admit it.

The Betz cells must contribute a very small proportion to the entire pyramidal tract, and lesions of their axons would not, therefore, constitute a very prominent feature

in these tracts, more especially if the lesion is no longer recent, and fails to respond to the Marchi test; in such a case the scattered degenerated fibres might easily escape detection. And, again, even when the degeneration is sufficiently recent to give the Marchi reaction, it does not affect the whole nerve-fibre sheath, but picks out apparently different levels in different fibres, so that cross sections of the cord give only an imperfect picture of the real amount of damage; in fact, often when longitudinal sections reveal a considerable amount of degeneration it is barely perceptible in cross sections. To get a true idea of the amount of degeneration in these slight cases it is necessary to examine a series of longitudinal sections. Judging from my own cases I am of opinion that the degeneration in the crossed pyramidal tracts in cases of alcoholic origin is sufficient to account for the state of the Betz cells.

S. J. Cole lays stress upon the selective action of the poison on certain cells, and would exclude the possibility of this action starting peripherally in the axon and affecting the cell secondarily. It does not seem to me that there is any greater difficulty in conceiving a selective action of the poison on the axons than on the cells of which they are a part. Anything which lowers the vitality of the cell will render its outlying parts particularly susceptible to deleterious agents. In reference to the influence one cell has upon another with which it is in association we have now considerable evidence in support of the idea that the deprivation of stimuli normally passing to one cell from another is sufficient to set up the change in the cell so deprived. According to Van Gehuchten[2] there is a marked distinction between the consequence of severing a motor and a sensory nerve. In both cases the cells of origin suffer, but whilst the motor cells generally recover, the spinal ganglia cells degenerate. He explains this on the assumption that after severance of peripheral nerves the motor cell remains under the influence of the trophic stimuli which comes to it from other cells with which it is in relation, whilst the spinal ganglia cells are deprived of these stimuli. From these experiments he concludes that the neurones which

stand in connection one with another also exercise a trophic influence on each other, and that this influence appears absolutely necessary for the maintenance of normal anatomical and physiological integrity.

Neither experimental nor pathological alcoholism results in cells which support the idea that the axonal change is the direct result of a toxic action of alcohol on the cells. Ewing apparently found axonal reaction cells in two cases of delirium tremens, but as he makes no mention whether the cord was examined for tract degeneration his observations are of no value for deciding this question.

I believe that we can adequately account for the cells showing this change by the two causes above considered, and that, at present, there is no necessity to invoke a third, viz., a direct toxic action.

In the case of alcohol among other poisons I regard the cell change as secondary to the fibre change, and I think that possibly by the determination of tract degeneration we may have a means for discriminating those cases, the result of axonal reaction (cases, *i.e.*, of central neuritis) from those where the change is the result of deprivation of the normal stimuli.

In all four of my cases (19, 28, 30, 32) where a large number of axonal cells were met with in the posterior ganglia, the posterior columns were markedly degenerated, and as experiments show that section of the posterior roots has no effect on the ganglia cells, I assume that in these cases the primary lesion was in the peripheral sensory nerves, and that the posterior column degeneration was secondary to the cell change.

Peripheral Chromatolysis with Central Nucleus.

Lugaro [2] found in the ganglia cells of dogs after arsenic poisoning a disappearance of the chromatoplasm all round the periphery, leaving a very restricted area of Nissl granules around the central nucleus, which together with the axis cylinder, appeared unaffected.

Marinesco [2] in similar circumstances found the cells showing axonal reaction.

I have frequently noticed in different cases cells presenting the condition found by Lugaro in arsenic poisoning. These cells (fig. 6) appear to have an extremely wide and irregular outer clear zone which, however, has a ragged or even reticulated aspect, and frequently, although the chromatoplasm is so diminished in quantity, yet its outer border still retains a well marked ring of large flakes. The cases which showed in my series the greatest number of cells in a state of axonal reaction also showed a very considerable number of cells with this peripheral chromatolysis. Arsenic is a poison which acts on the peripheral nervous system, and possibly both the changes noted by Lugaro and Marinesco are due to this action. If so, then we have altogether four different changes in the ganglia cells capable of being set up by injury to their axons.

Dark Staining of Cells.

In most ganglia some of the large and medium-sized cells stain intensely with toluidin blue, owing to the ground substance being coloured as well as the chromatoplasm. We must bear in mind, however, the effects of injury to the cells during removal, which, as I have already shown, produce a somewhat similar appearance. Nevertheless I do not think that this is the cause of the change in carefully extracted ganglia, because in the dark cells, which I take to be pathological, there are differences by which they can be distinguished from the injured cells, viz., excess of pigment; retention of outer dark ring of flakes, and less alteration in the size and appearance of the nucleus, which although it stains darkly, and more or less homogeneously, does not present the marked distortion and shrinking seen in injured nuclei.

In early stages, or when the cells are only slightly affected, they seem to have merely a greater affinity for the stain which colours not only the Nissl-granules, but the ground substance as well. In those more markedly affected there is much shrinking and distortion, they are very darkly stained, and often contain a large, well-demarcated mass of yellow pigment, and usually, but not always, the nucleus

is in a state of homogeneous degeneration. The outer clear zone is always absent. Finally, all that remains of the cell is a shapeless mass with a large space separating it from its capsule. When stained with erythrosin and toluidin blue it has a great affinity for the former and very little for the latter, so that it appears as a red mass with no internal detail, its nucleus blending insensibly with the cytoplasm, and of much the same colour. In this advanced stage it is no longer dark, and appears as a pale hyaline mass. The end stage of acute cell change apparently results in a similar condition; probably in both cases the cell no longer functions, and is dead.

I have only examined the ganglia in one case of tabes (No. 33), and found cells showing all the above changes, both very dark, shrunken, and pale, hyaline-looking cells. A similar condition was found apparently by Strœbe and Wollenberg[8] in the same disease.

Conjoined Cells.

It is quite a common occurrence to see two or even three apparently normal cells joined or closely applied to each other without any capsule between them. This condition is also commonly met with in the spinal ganglia of animals (cats). It is usually the small or medium-sized cells which are so joined. Along the part where the cells are in apposition there is a distinct line, on either side of which lies a narrow space with strands or threads passing across it from the line to the cell (see figs. 10 and 11). Having regard to the frequency with which this condition is met with in presumably healthy ganglia, and to the further fact that neither the cytoplasm or the nucleus show any morbid changes, it would seem as though this condition was physiological. Again, in very young kittens (three to five weeks old) it is a common occurrence to meet with three or four or more small facetted cells in one capsule, but as older animals are examined this condition gets less frequent, until in the adult it is comparatively rare. I have not, however, noticed in the case of young animals the

dark line separating the approximated cells. No mitotic figures appear in the nucleus, but on the whole the appearances certainly are very suggestive of cell division.

Nuclear Changes.

The most common and probably the most important is where the nucleus appears solid and homogeneous, and stains darkly. In the erythrosin and toluidin blue combination it shows a tendency to retain the former, and apparently as the change progresses so its affinity for erythrosin increases. It becomes also much diminished in size (see figs. 2 and 9). I have not, however, noticed with this change the shrivelling described by Orr, but sometimes it shows a distinct notch in its border. This is the condition described by Sarbo as homogeneous degeneration. It is not often that one comes across a ganglion which does not show instances; in many of my cases, however, it occurred in the majority of the cells. A similar condition I have noticed in cats, kittens, and puppies, and as already mentioned, injury, and probably very slight injury, is capable of producing a similar change. It is generally associated with a wide perinuclear space, and is apparently an early change, for very often the cytoplasm of cells which show it have a normal appearance. It almost constantly accompanies the dark-stained cells, and always those which stain red with erythrosin (probably dead cells), but in these, although still homogeneous, it is no longer dark.

The possibilities of its being in some cases a *post-mortem* result must also be borne in mind; unquestionably tissues kept unduly long before being fixed show a similar condition, but I think that, considering it is often most common in cases which have only been dead a few hours before the cells are fixed, and further that side by side normal and dark nuclei are met with, we must allow that even if it is, strictly speaking, a *post-mortem* result, yet still this shows itself, owing to some chemical changes, in the cell structure, the result of vital action, and that therefore it has in any case a pathological significance.

Occasionally crescents and "S" shaped lines staining darkly are seen within otherwise normal-looking nuclei; these are not common. They are referred to under the cases in which they were seen and I have no suggestion to make concerning their significance.

Sometimes the nucleus is dark and much shrivelled (see fig. 6) and has a wide perinuclear space according to the experiments of Hodge and others these would represent a fatigue form. Before leaving the cell changes I would just mention in reference to pigment, that sometimes in place of being deposited in a lump at one side, we meet with a definite ring of it encircling, at a little distance, the nucleus, or perhaps not completely surrounding it, and occasionally there are granules which stain a bright crimson colour (with erythrosin) among the usual pigment.

Changes Affecting the Supporting Tissues and Vascular Changes.

Interstitial hypertrophy and proliferation, general or in patches, is a very common feature. We have to differentiate between the overgrowth of the connective tissue and the cells of the capsule. The two are not necessarily involved together. Orr and Rows[1] have drawn attention to the very frequent increase of the capsular cells in general paralysis, and my cases also show this feature, but it is not limited to, and is not always present in even advanced general paralysis. In several of my cases (5, 20, 22) it was not noted, and one of the best examples I came across occurred in the case of an imbecile (17). The capsular cells are readily distinguished from the connective as they have much larger and more oval nuclei, which do not assume the elongated, bent rod like forms of the connective tissue. Some of the largest nuclei, however, of the capsule must belong to nerve-cells, which in their entirety are only revealed by special methods.

Localised patches of connective tissue overgrowth, surrounding atrophied remains of ganglia cells, are not infrequent in the cat.

In amongst the connective tissue a peculiar fine grained highly refractive pigment is occasionally met with which stains bright green with toluidin blue.

The little clumps of darkly stained nuclei in the spaces formerly occupied by ganglion cells form a prominent feature in many ganglia and must represent very considerable destruction of the nervous elements. Orr and Rows refer to them; they state that empty capsule spaces are always artefacts, but I doubt this as the ghost-like ragged remnants of nerve-cells are often met with occupying a small part of a large capsular space without any evidence of any capsular hyperplasm or connective tissue overgrowth in the neighbourhood.

The only changes which I have noted with reference to the vascular system beyond the very manifest thickening of the vessels in No. 14 are congestive changes, increase of leucocytes chiefly polynuclear, and intravascular separation of fibrin. The latter occurred in three cases (22, 29, 32). I have not infrequently noticed it also in the cortical vessels, especially of general paralysis. It occasionally forms masses enclosing amongst its meshes, leucocytes. W. O. Barrett[9] has recently drawn attention to its occurrence in the vessels of the false membrane in cases of pachymeningitis, hæmorrhagica interna.

I have recorded these observations with the conviction that the study of the changes in the spinal ganglia cells in connection with the changes of the cells of the central nervous system will give us a more intelligible conception of their bearings on the pathology of insanity. Our grasp of the subject will thereby be more comprehensive and more accurate. It becomes evident even from the few cases here collected, that although an examination of one part of the nervous system may give quite negative results, that when we extend the scope of our investigations this will much less frequently happen.

Hitherto our attention has been too much restricted to the efferent or motor side of the nervous system, although there is no reason why lesions or defects of the afferent or sensory should not equally participate in the pathology of insanity.

My thanks are due to my colleague Dr. de Steiger for assistance in preparing and examining some of the material made use of in this paper.

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Description of the Figures.

Fig. 1.—(× 600.) From Case 14. Represents one of the healthier cells of a ganglion. In this instance there was no indication of axonal reaction, but probably commencing acute cell change. Notice the well marked outer clear zone and the peripheral ring of large dark flakes, and the clear central nucleus with no perinuclear space.

Fig. 2.—(× 450.) From Case 18. The clear outer zone extends quite up to the capsule, internal to it is a very prominent ring of large dark flakes with a narrow clear zone again along its inner surface. The remaining granules are large and distinct; the slightly paler patch to the right represents pigment. The nucleus is very small and dense, very little larger than the nucleolus which is clearly seen in the original but not in the print. The perinuclear space is very wide and shows a faint reticular appearance. The nucleus is that part of the cell which alone shows decided pathological appearances (homogeneous degeneration).

Fig. 3.—(× 450.) From Case 30. Extreme chromatolysis and homogeneous degeneration of nucleus. No perinuclear space. The nucleolus exists as a pale red body not shown in the print but visible in the negative. This condition represents one of the changes the cell undergoes after the severance of its peripheral axon.

Fig. 4.—(× 450.) From Case 28. A cell in a state of axonal reaction with peripheral nucleus which slightly bulges the cell contour; the nucleus is not diminished in size and appears fairly normal; it is bordered at one part by a dark rim of chromatoplasm. The cell is bordered by a more or less complete band of dark flakes and has no clear outer zone.

Fig. 5.—(× 450.) From Case 28. This also represents one of the changes the cell undergoes after severance of its peripheral axon. The nucleus is not markedly displaced but is indistinctly outlined and small, and surrounded by a small dark area of fine granules which insensibly fade into the pale

washed out cytoplasm of the main body of the cell. There is the remains of a peripheral ring of dark flakes but no clear outer zone.

FIG. 6.—(× 450.) From Case 28. Marked peripheral chromatolysis with central nucleus. Notice the very broad flimsy outer zone which is not homogeneous as in Fig. 1, but has an indistinct reticular appearance with a more or less distinct dark outer border. The chromatoplasm occupies quite a small area and consists of fine grains, closely packed and showing in this instance no outer rim of larger flakes. The nucleus is dark and puckered but not homogeneously stained; it is surrounded by a well defined perinuclear space. The axis cylinder is extremely attenuated and can be traced as a slightly darker band through the outer rim to the retracted chromatoplasm.

FIG. 7.—(× 600.) From Case 13. Acute cell change with rather dark staining of cytoplasm. No definite Nissl granules to be seen. A clump of pigment lies at the extreme right of the cell. Notice the smooth contour of the cell, its central and rather indistinctly defined nucleus and swollen nucleolus. There is complete absence of both outer clear zone and perinuclear space. The axis cylinder is extremely attenuated and stains more darkly than in the normal condition.

FIG. 8.—(× 600.) From Case 8. Acute cell change with very pale staining and slightly darker border. The nucleus blends almost insensibly with the cytoplasm. The nucleolus is large. The axis cylinder attenuated.

FIG. 9.—(× 450.) From Case 18. The cell to the left is darkly stained, shrunken and distorted, with no outer clear zone but a continuous band of chromatoplasm. Although the cytoplasm is coloured generally, yet the Nissl granules can still be seen (contrast this with the cell above) especially closely clustered about the nucleus. There is a large circumscribed patch of yellow pigment at the lower end, and the thin axis cylinder springs from this region. The nucleus is denser than normal, not manifestly shrunken and with barely any perinuclear space. The cell on the right shows a fairly normal disposition of its constituent cytoplasmic parts, but its nucleus is very small and homogeneously stained and lies in the midst of a wide perinuclear space in which can be seen a delicate reticular structure.

FIG. 10.—(× 600.) From Case 5. Two small cells in apposition. Notice the clear space between them along the centre of which runs a thin dark line. These cells apart from being rather heavily pigmented have a fairly normal appearance. They have no definite clear outer zone but only a few threads radiating towards the capsule. The cytoplasm is bordered by a well defined ring of dark flakes and there is no perinuclear space.

FIG. 11.—(× 600.) From Case 20. Three cells in apposition. The dark line between them is well shown.

PLATE I.

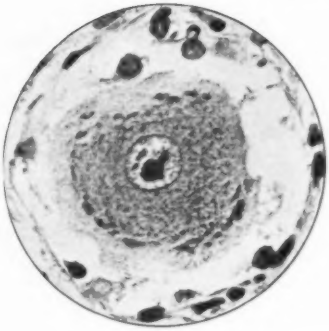


FIG. 1.

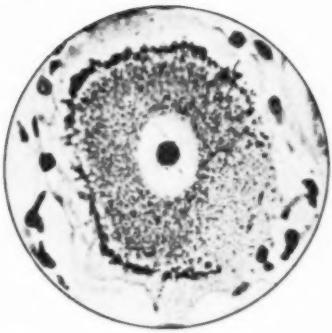


FIG. 2.

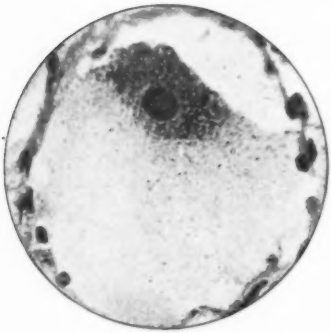


FIG. 3.

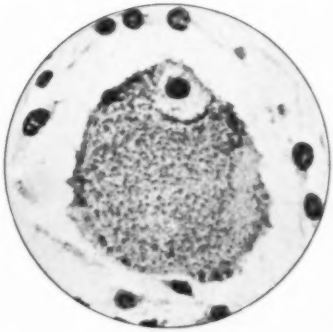


FIG. 4.

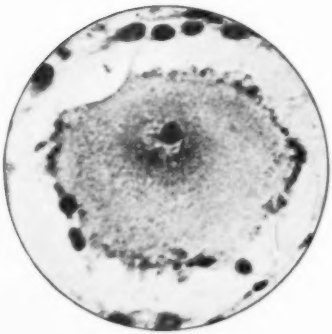


FIG. 5.

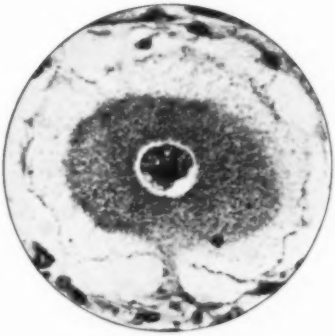


FIG. 6.

PLATE II.

FIG. 7.

FIG. 8.

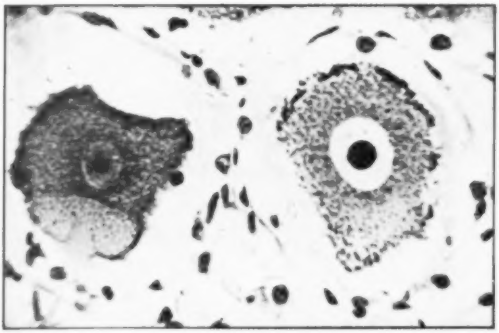


FIG. 9.

FIG. 10.

FIG. 11.

ON THE DIAGNOSTIC VALUE OF THE POSITION OF THE HEAD IN CASES OF CEREBELLAR DISEASE.

BY FREDERICK E. BATTEN, M.D.

Introduction.

It has been shown by Dr. Risien Russell[1] that after experimental ablation of one lobe of the cerebellum the animal tends to assume a very different attitude. This is described as follows: The trunk is curved with the concavity to the side of the cerebellar lesion, the side of the face is approximated to the shoulder on the same side; there is a rotation of the neck, so that the side of the face corresponding to the cerebellar lesion is turned upwards, and the chin is directed to the unaffected side.

The questions with which this paper deals are: (1) Is a definite attitude of the head assumed in man in cases of cerebellar disease? (2) Does the position correspond to that produced by experimental lesion, and if so, can the sign be used as a symptom of diagnostic value? (3) Is the position assumed in cases of intracranial disease in which no gross lesion of the cerebellum can be found?

In dealing with these questions it must be pointed out that in the large majority of cases of cerebellar tumour at the time of death the growth is so large and involves structure in the neighbourhood of the peduncles, or of the pons, that they cannot be brought forward as evidence of the production of a definite attitude; for, although in many cases a reasonable guess may be made as to the probable point of origin of the tumour, yet it is but a guess, and hence of little scientific value. My excuse for discussing the question from

[1] *Trans. Phil. Soc.*, 1894.

the standpoint of a single case is that this case alone, of numerous cases which I have seen, has had a lesion so localised and quiescent at the time of death that it had failed to give rise to any symptoms for many months before the death of the patient, and yet during its active stage gave rise to a very definite group of symptoms.

This absence of symptoms during the latter period corresponds with what might be expected from experimental evidence, for animals in which one lobe of the cerebellum has been removed exhibit but few symptoms after the lapse of a few weeks.

(1) *Is a Definite Attitude of the Head assumed in Cases of Cerebellar Disease?*

There is no doubt that in many cases of cerebellar disease a definite attitude is often assumed which may be present for some time, but is not necessarily present during the whole course of the disease. In six cases, which I had the opportunity of investigating pathologically, a characteristic position was present in three, while in the remaining three no special position of the head was assumed.

(2) *Does the Position correspond to that produced by Experimental Lesion, and if so, can the Sign be used as a Symptom of Diagnostic Value?*

To bring forward evidence on this point is the main object of the paper, for it is difficult in many cases of cerebellar tumour in which the growth has been extensive to be certain whether the position assumed has been due to the lesion itself or to pressure on structures in the immediate neighbourhood.

The following case furnishes evidence on this point which is free from such objection :—

M. R., aged 5 years, was quite well till she had measles in April, 1898. In July, 1898, she began to complain at times of severe pain across the forehead, she used to vomit after these attacks, and after vomiting the headache was better. The

attacks of headache generally occurred in the morning and lasted about 15 minutes. After November, 1898, the attacks of headache and vomiting became less frequent, and about this time the sight began to fail in the left eye, and she said that things appeared black. Her gait became unsteady and she frequently fell—generally backwards. She became deaf for two or three days, but then completely recovered her hearing.

Family history.—The patient was the youngest of five living children, all of whom were healthy. One child, 8 years old, died of consumption four years ago, *i.e.*, when the patient was 1 year old. The mother and father were perfectly healthy, but the mother had lost a sister from consumption. The child was first seen as an out-patient at the Hospital for Sick Children, Great Ormond Street, in January, 1899. She was nearly blind, she walked fairly steadily, but with the timidity of a blind person in a strange room. When standing or sitting she held her head to one side, so that her left ear was approximated to her left shoulder; her face was turned to the right, and the chin was slightly elevated; there was a slight spinal curve, with the concavity to the left. The eyes were noticed as tending always to the left, and did not come over easily to the right. The incoördinate movements of the right side were more marked than those of the left, but there was no loss of power. The knee-jerk was obtained on the left side, but not on the right.

In January, 1899, she was admitted to the hospital, and the following note of her condition was taken. The child was well nourished, but rather pale. She sat up in bed with her head in the position above described (see photograph, fig. 1) but the position was not constantly maintained, although there was always a tendency to revert to that position. She walked very unsteadily and kept her legs wide apart, and could not stand without a little support. (The discrepancies between the condition of the gait as noticed in the out-patient room and that noted in the ward is, I believe, explained, not by the fact that disease was progressive, but by the fact that when the child was brought to the hospital she had been walking about, whereas when the note was taken in the hospital, she had been in bed for a few days.)

In children who have *just* learnt to walk, and in whom some slight feverish condition has necessitated their being kept in bed for a few days, it is often noted how unsteady is their gait when they are first put on their legs, and children are not infrequently brought to the hospital with the history of having lost power in their legs after some febrile illness whom, on examination, present

no true loss of power but show merely an unsteadiness of gait. So in the present case the incoördination was brought out by want of use.

The child was quite intelligent and answered questions well. She could repeat short nursery rhymes. Her perception of light was doubtful. The right pupil was larger than the left, both were large and reacted feebly to light. Nystagmus was more marked when the child looked towards the left than when looking towards the right. There was no squint or paralysis of ocular muscles. There was slight facial weakness of the left side, but hearing on the two sides was equal. There was a general unsteadiness of the hands, but the intention tremor and incoördination was more marked on the right side than the left, and the grasp of the left hand was better than that of the right.

The same weakness was noticed in the right leg when the patient attempted movements against resistance. When stood with her eyes shut and her feet close together, she on the first occasion fell backwards, and on the subsequent trials fell to the left. The knee-jerks were not easy to obtain, but the left was greater than the right. The plantar reflexes gave flexor responses. Sensation was normal to all forms.

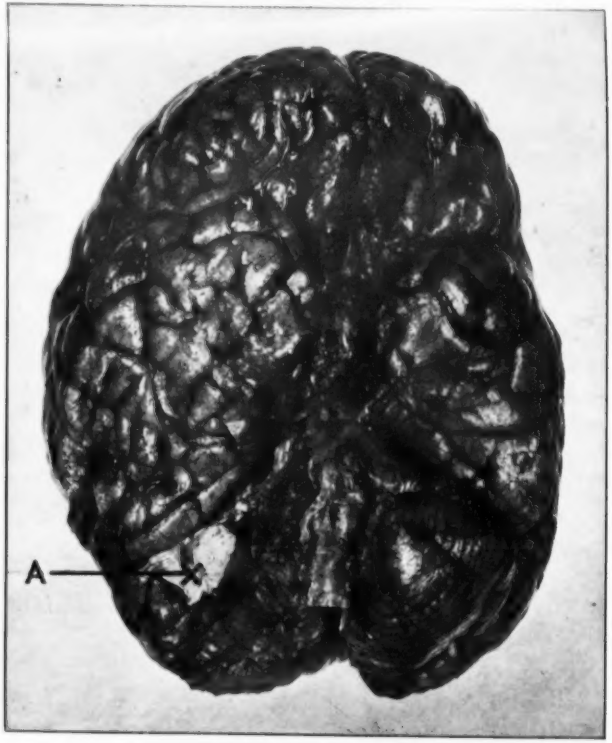
The child had one attack while in the hospital. She suddenly called out that she felt giddy and fell forward (at the time she was sitting on the locker at the side of her bed). When asked to walk alone, she said she could not as she would fall forward. She would not lie down as she said it made her feel giddy. There was no vomiting immediately after this attack, and she complained of no headache. In the evening of the same day, however, she vomited.

She left the hospital at the end of January, 1899, but returned again as an out-patient in September of the same year, with a swelling of the left elbow joint, which was undoubtedly of a tuberculous nature.

She had during this period remained in good health, had had neither headache nor vomiting, and could skip and swing in the garden. She could walk well without staggering. The position of the head was natural. There was but slight incoördination and intention tremor of the right hand. The left knee-jerk could just be obtained, the right could not be obtained; the plantar reflexes both gave flexor responses.

The child now passed from my care to that of my colleague, Mr. Horace Collier, for treatment of the tuberculous elbow, but I had the opportunity of seeing her from time to time.

FIG. 1. — Photograph of child, showing position of head assumed in a lesion of the right lateral lobe of the cerebellum.



× *Dura mater adherent to tumour in cerebellum.*

FIG. 2.—Photograph of base of brain. The right lobe of the cerebellum has been somewhat torn during removal of the brain from the calvarium. The X shows the spot where the dura mater was adherent to

In January, 1901, she was very well. She walked steadily. There was still slight incoördination of the right arm—and her mother stated that she had perception of light. Both knee-jerks were obtained. The head was held in a natural position, and the the right occipital region was noted as being somewhat more prominent than the left.

In November, 1901, she was in good health. She was going to the blind school and enjoyed her lessons. She was a most intelligent child.

Early in 1902 her mother developed phthisis and died. On August 6, 1902, I was asked to see the child at her home with Dr. South. She had remained well till six days previously, when she became very quiet, had bleeding from the nose, but complained of no headache or vomiting. Two days previously she had had a convulsion, which lasted a few hours, and her temperature rose to 103°. She was unconscious for some time afterwards.

On examination on August 6, she was conscious, could answer questions, put out her tongue, and move her arms and legs well. Her heart was acting very rapidly. There was no optic neuritis, and the knee-jerks were obtained with difficulty. There was a return of the convulsions during the evening, and she died on the following day. Leave for an autopsy was given and it was performed twenty-four hours after death.

The brain and spinal cord were alone examined. The surface of the brain was congested, but there was very little flattening of the convolutions. There was some opacity of the membrane over the base of the brain, and some matting of the Sylvian fissures and evidence of recent tuberculous meningitis. In the posterior fossa of the right side adherent to the dura mater over the petrous bone was a hard calcareous mass, about the size of a hazel nut. This mass lay in the substance of the right lobe of the cerebellum, and owing to the close adherence with the petrous bone, the cerebellum could only be removed from the calcarium by tearing its substance (see photograph of base of brain, fig. 2).

After hardening in formalin the brain was cut by horizontal sections. The ventricles appear normal, and nothing abnormal could be noticed in the internal capsule. On examination of the right optic thalamus it appeared rather mottled in appearance and slightly harder than

normal, and it was thought that this might show some tubercular process; subsequent microscopical examination, however, proved that there was no disease of the optic thalamus.

Sections through the cerebellum showed no departure from the normal, except the loss of substance produced by the tuberculous mass on the right side; the pons and medulla appeared normal.

The membranes over the posterior surface of the spinal cord were thickened and slightly opaque, but there was no exudation.

On microscopical examination, no change could be found in the spinal cord, and there was no evidence of degeneration in the posterior column—neither recent nor old. There was, however, evidence of thickening of the membrane, not only on the posterior surface, but also on the anterior surface.

The tuberculous meningitis was evidently of some standing, and affected not only the brain, but also the spinal cord.

In this case then, it has been shown that a definite position of the head was assumed in the case of the tumour of the right lobe of the cerebellum—that position being with the left ear approximated to the left shoulder, the chin raised, and the face looking to the right. In so far then, as the approximation of the left ear to the left shoulder is concerned, it is the reverse to the position seen in dogs after experimental ablation of one lobe of the cerebellum, but in so far as the position of the face and chin are concerned, it is the same as that assumed in dogs.

It would serve no useful purpose to enter into a discussion on the difference of position as seen in this case and that seen in experimental ablation. The influence of the cerebellum on the tonus of muscles is well known, as shown by the work of Horsley, Lowenthal and Sherrington, and the difference between an ablation experiment and a slowly growing tumour readily suggest a so-called paralytic and an irritative lesion. The difference between the prone position of a dog and the erect position of man may have also to be brought into consideration.

The following tabular statement shows in a concise

manner the symptoms as observed in an experimental lesion compared with those seen in this case :—

Ablation of the right lobe of cerebellum (from Dr. R. Russell).	Tumour of the right lobe of cerebellum.
Rotation to the left (in-going corkscrew).	
Reeling to the left.	Fell to left (generally).
Attitude.—Right side of face turned up and to the right, the right ear approximated to the right shoulder.	*Attitude.*—Right side of the face turned up and to the right : *left* ear approximated to left shoulder.
Concavity of the spine to the right.	Concavity to the left.
Incoördination of right side.	Incoördination of right side.
Rigidity.—Right side.	
Reflexes exaggerated most on right side.	Knee-jerks.—Right absent ; left present, diminished.
Weakness right side and posterior limb of opposite side.	*Weakness* slight of right side.
Anæsthesia and analgesia same as motor paresis.	None.
Deviation of left eye-ball downwards and outwards.	Tendency of eyes to turn to the left.
Lateral nystagmus to the right.	Nystagmus most marked to the left.

It will be noticed, by comparing the above tables, that the symptoms observed in this case which corresponded to those which might be expected from the ablation experiments were : the tendency to fall to the left, the incoördination of the right side, and the weakness of the right side. The position of the head corresponded so far as the turning of the face was concerned, but the approximation of the side of the face to the shoulder was on the opposite side to that seen experimentally.

The signs which were the reverse of the experimental lesion were : the diminution of the knee-jerk on the right side, and the more marked nystagmus on deviation to the left, and the concavity of the spine to the left. The rotation, the rigidity, the anæsthesia and analgesia, and the deviation of the eyeball present experimentally, were not present in the clinical case.

The absence of the knee-jerks in cerebellar tumour is rather the exception than the rule. In the present case the right was absent and the left diminished throughout nearly the whole course of the disease.

The degeneration of the posterior column and the posterior roots might have afforded an explanation of the

condition. On the other hand, the pathological examination of the cord revealed no degeneration of the posterior roots or posterior column. There was, however, considerable thickening of the membranes of the cord on its posterior aspect—this thickening, although not of recent origin, yet had not the appearance of having been present for some years. That the absence or presence of knee-jerks does in some measure depend on the degeneration of the posterior column and posterior roots in many cases of cerebral tumour is certainly probable, but this explanation does not hold in the present case.

Before passing to the discussion of the next question, it may be noted that of the six cases of cerebellar tumour above referred to, in three the right ear was approximated to the right shoulder, and in these a lesion of the left lateral lobe was found on *post-mortem* examination.

(3) *Is this Position Assumed in Case of Intracranial Tumour in which no Gross Lesion of the Cerebellum can be found?*

The following case may be quoted as an instance in which the head assumed a definite posture, and no tumour of the cerebellum was found to be present on *post-mortem* examination.

V. P., aged 7 years, was admitted to the Children's Hospital under the care of Dr. Penrose in September, 1900, and to him I am indebted for permission to make use of the notes of this case. The history was that three months previously he had been quite well. He then began to complain of headache, had vomiting, was delirious at night and began to get thin.

He was the eleventh of eleven children. There was no evidence of syphilis or consumption in the family. On admission to the hospital he was a thin, poorly-nourished boy, and complained of frontal headache on the left side. The pupils were large and reacted sluggishly to light. The margins of the discs were not quite clear, but there was no definite optic neuritis. There was nystagmus on conjugate deviation of the eyes to the right. There was no ocular palsy. The boy when standing was unsteady and tended to fall backwards. He held his head with the right ear

approximated to the right shoulder and the face looking towards the left, and the chin well forward.

There was no prominence of the skull in the occipital region. There was no incoördination of the arms or legs, but the right leg seemed slightly weaker than the left.

The knee-jerks were active and equal, and there was a tendency to ankle clonus, and the plantar reflexes gave flexor responses.

No disease of the thorax or abdominal viscera could be detected. There was considerable hyperæsthesia of the skin all over the trunk.

During the next three months he continued to have most severe attacks of headache and vomiting, with rise of temperature after the attack. He would have one of these attacks about every three days.

His symptoms remained practically unaltered; there was no increase of weakness, except that due to progressive emaciation. The position of the head was not constantly maintained.

The boy died some three months after admission to the hospital.

At the *post mortem* there was very marked flattening of the convolutions, which were pale and sticky, there was no evidence of meningitis, although the tips of the temporo-sphenoidal lobes were adhering to the dura mater. The membrane between the medulla and the cerebellum in the region of the fourth ventricle was thickened, and so marked was the thickening that it appeared possible that there might be a small tumour in this situation. On microscopical examination, however, this mass was shown to consist only of inflammatory tissue. Protruding to the right of the medulla was a small cyst, which was shown by subsequent examination to be due to distention of membrane from the side of the fourth ventricle.

On opening the ventricles, they were found to be enormously distended, and the distention extended through the iter into the fourth ventricle.

The cerebellum on section appeared normal. The thoracic and abdominal viscera were normal.

The spinal cord was normal, both on microscopic and macroscopical examination.

There is little doubt that this was a case of hydrocephalus due to blocking of the foramina in the region of the fourth ventricle. The case proves, however, that the peculiar position of the head may be assumed in cases in which no tumour of the cerebellum is present.

Summary.

It may be stated in answer to questions with which the paper proposed to deal:—

Firstly.—A definite attitude of the head is not infrequently seen in cases of cerebellar disease in man, that position being with the ear approximated to the shoulders on the side opposite to the lesion, and with the face turned up to the side of the lesion.

Secondly.—This position of the head, so far as the approximation of the ear to the shoulder is concerned is the reverse, while the position of the face is the same as that seen after experimental ablation of one lobe of the cerebellum.

To answer the second portion of the question, viz., can the sign be used as a symptom of diagnostic value? in the bare affirmation might lead to error, for the relative value of this symptom in comparison with the other symptoms of a cerebellar lesion, is a question which needs most careful consideration in each individual case. It is probably a symptom of less importance than incoördination or weakness.

Thirdly.—The fact that the position is sometimes present in cases in which there is no gross lesion of the cerebellum is a further reason for not attaching too great importance to the position assumed by the head.

In conclusion.—It may be said that as an additional and confirmatory sign of cerebellar tumour, the position assumed by the head is of value, but too much importance should not be attached to its presence alone, or when opposed to symptoms which have been shown to possess greater diagnostic value.

ON THE LOCALISATION OF A RESPIRATORY AND A CARDIOMOTOR CENTRE ON THE CORTEX OF THE FRONTAL LOBE.

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AND

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THE respiratory disturbances occurring in hysteria, dementia paralytica, and many other diseases of the central nervous system, have in this clinic been studied for a long time under the direction of Professor Winkler. It very soon became apparent that fixation of attention greatly influences the type and rhythm of respiration.

A detailed investigation concerning this matter by Winkler on presumably normal persons showed that concentration of attention is always associated with a definite group of phenomena. In the first place shortening of the time of expiration, which at the same time becomes more superficial; the same holds in a less degree for the inspiration, while the thorax is more and more brought into the inspiratory position. When attention is relaxed a compensating retardation of respiration sets in, again chiefly affecting the expiration, with a tendency to deeper expiration at longer intervals.[1]

As a second attribute of fixed attention acceleration of the pulse is found. This acceleration starts almost immediately, and is, with relaxed attention, followed by a compensating retardation. As a third characteristic of concentrated attention extremely small extensory movements of the fingers and of the neck were observed.

[1] Winkler, "Attention and Respiration," *Proc. R. Acad. of Sciences*, Amsterdam, 1898, October 29, p. 133.

It was these small extensory movements in the syndrome accompanying fixation of the attention in connection with Spencer's[1] investigations on the influence of the cerebral cortex on the type of respiration which induced us to attempt, if it were possible, to call forth the whole of this syndrome of symptoms, or each symptom separately, from a definite part of the cerebral cortex. The experiments were for the greater part made on dogs, and showed that at the top of the sigmoid gyrus, where the coronal and pre-sylvian fissures meet, a small field is situated, about two millimetres long and equally broad, from which, on stimulation with a very weak faradic current, accelerated respiration and inspiratory position of the thorax are obtained.[2] Further research[3] showed that in many individuals these two functions are not located in the same place, but that from that part of the field which lies more at the top of the sigmoid gyrus, acceleration of respiration is exclusively or principally obtained, and, when the respiration has already reached a high frequency, predominantly deepening of the respiration; whereas that part of the field which lies more backward towards the crucial fissure, causes exclusively the inspiratory position of the thorax. This little field borders immediately on the region from which Ferrier and others obtained stretching of the neck and movement of the head towards the contra-lateral side. When successive sections of the brain were cut off both functions could be followed along paths which diverged more and more as the internal capsule was approached. The path along which inspiratory position of the thorax is obtained proceeds with the pyramidal fibres through the internal capsule. There they lie in the part which is most turned to the front, and can be traced as far as in the pyramidal tract. The path along which accelerated rhythm is obtained forms in front of the head of the caudate nucleus a closed system which has its place in the anterior

[1] Spencer, *Philosoph. Transact. Royal Soc.*, London, 1894. A complete survey of the literature about the influence of the cortex on the respiratory type can be found in the dissertation of Dr. W. Beckmann, 1899.

[2] Winkler and W. Beckmann, *Proc. Royal Acad. of Sciences*, Amsterdam, 1899, March 25.

[3] Beyerman, *ibid. Proc.*, 1901, April 20.

limb of the internal capsule. This path could be further traced as far as the medial nucleus of the optic thalamus by Schüller.[1]

In order to control these stimulation experiments, we extirpated in dogs the above-mentioned cortical field unilaterally. The operation was performed under rigorous aseptic precautions, and recovery always proceeded very favourably. Immediately after the operation respiration is irregular, greatly retarded, and repeatedly interrupted by deep sighs. After a few days these sighs disappear, breathing becomes more regular, its frequency gradually increases. After from ten to twelve days compensation is complete. During the period in which respiration is still very irregular, and repeatedly interrupted by sighs, it appeared that as soon as the dog fell asleep these signs and irregularities ceased, and the respiratory frequency rose.

On account of the experiments mentioned, it is very probable that at the top of the sigmoid gyrus in the dog a small field is situated, which, when stimulated, causes acceleration and deepening of the respiration and inspiratory position of the thorax, whereas extirpation of this part of the brain causes temporary retardation of respiration with irregularity and sighs, which disturbances disappear for the greater part during sleep.

The experiments undertaken with a view to show cardiomotor centres[2] also on the cortex of the brain, were less successful. Many writers, among whom are François Franck and Pitres[3] have noticed cardio- and vasomotor effects from various parts of the motor cortex and adjacent regions, but localisation in a definite part of the cortex appeared not to exist in their experiments. Also the experiments of Schäfer and Bradford[4] yielded the same results. Richet[5] on the other hand claimed that these functions could in the dog be

[1] Schüller, *Centralblatt f. Physiologie*, 1902, Bd. xvi., p. 223.

[2] In order to avoid confusion, we point out that when we speak of centres we do not imply a definite anatomical conception, and simply call centre of a certain function that spot on the cerebral cortex from which the smallest stimulus—with respect to its intensity as well as to its extensity—is able to evoke the function in question.

[3] François Franck, "Leçons sur les functions motrices du cerveau," 1887.

[4] "Textbook of Physiology," 1900, vol. ii., p. 714.

[5] *Thèse de Paris*, 1878.

chiefly localised in the anterior part of the sigmoid gyrus. Experiments by Winkler[1] show that the same spot which on stimulation causes a change in respiration, also causes very clearly an increase in the frequency of the heart attended with contraction of the vessels (determined in the femoral artery). The very important question how far the alteration of the frequency of the pulse on stimulation of the cortex is here to be connected with separate fields, has not been solved yet, but in the main Winkler's result agrees with Richet's. These experiments make it at least probable that on the cortex of the dog's brain, namely, at the top of the sigmoid gyrus, also a cardiomotor centre is to be found.

Guided by a couple of clinically observed cases, we hope to be able to locate the place of these two centres on the cortex of the human brain.

Historia morbi, No. 618.—Patient, J. v. G., female, aged 16 years entered the ward on account of headache, vomiting and impaired sight. Examination led to the diagnosis of tumour cerebri. Considerations upon which we cannot dwell here, made it probable that the tumour was situated in the left frontal lobe. The diagnosis was by no means certain. Increasing headache, accompanied by vomiting and imminent blindness, as a consequence of optic neuritis, induced us to proceed to an operation, mainly as a palliative. After the skull had been opened, there appeared to exist a very great tension within the dura. The dura was cleft, which laid bare the lower two-thirds of the anterior central gyrus, the adjacent base of the medial frontal gyrus, and the upper border of the inferior frontal gyrus. In that place no tumour was found.[2] Through the wound in the dura prolapsus of the brain substance occurred during the operation. In order to be able to close the dura it was necessary to amputate part of the brain. This part was the base of the medial frontal gyrus, where it borders on the anterior central gyrus and probably also the upper part of the inferior frontal gyrus where this latter borders on the anterior central gyrus. After the operation speech was disturbed. In a month's time this disturbance had so far improved that only a slight paraphasia remained. The general condition was considerably improved after the operation. Immediately after the operation

[1] *Loc. cit.* Fig. xxiv-xxviii.

[2] The patient died December 18, 1902, and a large tumour was found in the white substance of the left frontal lobe.

one was struck by the very irregular respiration, now and then interrupted by sighs. The curve reproduced in fig. 1 shows part of an observation registered[1] three days after the operation. This curve has a great resemblance to the curves which we obtained from our dogs after having extirpated a very limited part of the cortex (fig. 2). The course of compensation was difficult to follow owing to external circumstances. Moreover, what had happened was of too radical a nature to expect a pure result here. After about a month respiration had completely returned to its normal type and frequency.

We have briefly mentioned this case in order to show that also in man, when part of the second frontal convulution bordering on the anterior central sulcus is unilaterally destroyed, temporary respiratory disturbances occur closely resembling those which we observed in our dogs after extirpating a very limited part of the brain.

The second case was more suited for observation and we could follow it for a long time.

Historia morbi, No. 364.—Patient, J. K., entered the Neurological Clinic for epileptic fits, on June 14, 1897. He was then 16½ years old, a pale, delicately-built boy. He is of a nervous family, from father's as well as from mother's side, but decided nervous diseases do not occur in the family on either side. Abuse of alcohol exists neither in the father nor the mother. The child was normally born, got its teeth, and learnt to walk and speak in due time. When three years old he fell against a stove while playing, which caused two very small, insignificant wounds on the left side of the scalp. In that same week the child got scarlet fever, and on the spot of the wounds large abscesses developed, together with two abscesses in the neck. The abscesses were opened by a physician, much pus being discharged, especially from the abscesses on the scalp. After that the child was troubled with convulsions, in which it first turned pale, then blue, set its teeth, and showed spasms round the mouth. A few years afterwards nocturnal incontinence of the urine showed itself. At the age of about 13 clearly pronounced epileptic fits set in.

The fit is mostly preceded by an aura, during which the patient has a feeling of cold all over his body; sometimes the aura is

[1] The tracing of the respiratory movement was always done by means of a Marey pneumograph on a rotating cylinder. The tuning-fork always made 2 vibrations a second.

absent and the boy falls to the ground at once. The face is pale at first, later blue. At the same time movements round the mouth are noticed, as of one who attempts to speak; generally some inarticulate sounds are uttered. After that swallowing movements occur, the convulsions are spread over the whole face, the eyes are shut and the head turned to the right.

The pupils are dilated and the eyes deviate conjugately to the right. Next the arms are stretched, a fist is clenched, and by bending the wrist-joint flexed dorsally. The legs are drawn up. Sometimes rolling movements occur, but clonic spasms are generally absent. The tongue is not bitten and the urine rarely passed. The duration of these fits is very different, seldom exceeding ten minutes. After the fit the patient is for a moment confused, then sleepy with a feeling of pressure in the head. The minor fits assume the form of absences with spasms round the mouth and slight deviation of the eyes to the right. The fits occur during the night as well as in day-time, and are very different in severity and number.

When entering the hospital he showed no striking abnormal signs except the cicatrices on the skull. Heart, lungs and abdominal organs seemed normal, it only was remarkable that the frequency of the pulse always varied between 80 and 100 a minute and increased by pressure on the scars. Both the cicatrices on the frontal skull form deep impressions of which the bottom is formed by a very resistent, fibrous, cicatricial tissue having a white glossy skin, with loss of hair. Both scars are separated by a bony bridge. By means of Winkler's method[1] we determined the part of the surface of the brain corresponding with the scars. They proved to correspond with the base of the medial frontal gyrus not far from the place where the convolution borders on the anterior central gyrus. On July 1 the patient was removed to Prof. Korteweg's department, where the operation took place on July 9. In the account of the operation we find what follows. On the spot where the cicatrices are found on the skull, the dura mater showed a hyperæmic seam. By two cuts in the dura a triangular patch is formed, which appears not to adhere with the underlying pia. The pia mater was œdematous in that place, the brain itself seemed normal. Thereupon the patch of the dura was sewn and the skull closed.

Until July 27 the patient remained quite free from fits, then spasms of the face occurred for the first time. On August 2 the

[1] Winkler and Rotgans, "l'Etat actuel de la chirurgie nerveuse. Pays-Bas," p. 4 *Travaux du Laboratoire de Chipault*, 1900.

patient was dismissed, and thereupon a slight fit followed on August 7. The operation having produced little change in his condition, the patient was again admitted from January 11 to January 29, 1898. After that he came back again on November 30, 1900, complaining of the increasing number of fits and of slight weakness of memory.

Examination of the patient revealed what follows. The patient is about 21 years old, a pale, delicate boy. His face is slightly asymmetrical; the right eye-brow is somewhat lower than the left one, the right nasolabial fold seems more superficial than the left one, also the right corner of the mouth is somewhat lower. The motility of the face seems a little better on the left than on the right, excepting the left frontal muscle, which cannot very well be drawn up. On the whole the deviations are too slight, however, to draw any certain conclusions from them. The movements of the eyes show no deviations. The cornea-reflex is normal, the pupils react to light and by convergence and are wide and very varying in size. The fundus oculi shows no morbid deviations, the field of vision is not reduced. The tongue and jaw reflex are normal. Hearing, smell, taste are intact. No sensory disturbances. The arms show no striking deviations, strength pretty equal on both sides, muscular tone normal, no rigidity, the tendon reflexes pretty strong, no ataxia; a slight tremor in the fingers.

The thorax is long and flat and shows slightly dilated veins which shine clearly through the skin, especially on the left side, and pass on to the left arm and there become less distinct. Percussion and auscultation show no deviation of the lungs. The lung-liver line, which is easily movable, stays in the papillar line at the height of the upper edge of the seventh rib. On the back the borders of the lungs are in the scapular line at the height of the spine of the eleventh thoracic vertebra. The heart beat can just be felt in the fifth intercostal space in the papillar line. When the patient stands upright, distinct pulsations in the epigastrium can be noticed. On percussion of the heart no dulness is found, damping of the heart begins at the lower edge of the fourth rib, and does not reach beyond the right border of the sternum. On auscultation the sounds of the heart are normal. In the abdominal organs no disturbances can be detected. The back is normal; the abdominal and cremaster reflexes rather strong. The legs show no striking deviations, are of about equal size, the muscular tone is normal, there is no rigidity, tendon-reflexes are brisk, but there is no clonus or any indication of it.

Table I.

	Temperature.				Pulse.		Respiration.		Fits.	
	M		N		M	N	M	N	Major.	Minor.
	8	12	4	8						
June 14 to July 1, 1897	36·7	—	36·9	—	—	—	—	—	—	—
July 2 to July 9, 1897	36·7	37·0	37·0	36·9	101·3	80	21·3	21·5	—	—
July 10 to July 20, 1897	36·7	37·2	37·2	37·5	103·4	93·8	22·6	22·6	—	—
July 20 to Aug. 2, 1897	36·6	37·1	37·1	37·2	101·1	101·9	20·1	21·2	—	—
Jan. 11 to Jan. 29, 1898	36·8	—	36·9	—	—	—	—	—	—	—
December, 1900	37·0	37·3	37·3	37·2	110·6	106·5	23·9	26·3	4	7
January, 1901	37·1	37·3	37·5	37·2	117·0	109·8	23·9	23·8	1	25
February, 1901	37·1	37·3	37·4	37·4	114·0	111·0	22·1	23·7	1	10
March, 1901	37·1	37·3	37·5	37·5	108·9	114·5	22·3	25·5	0	14
April, 1901	37·0	37·3	37·5	37·6	107·7	112·2	22·7	26·0	4	8
August, 1901	37·3	37·2	37·4	37·5	118·0	108·4	22·2	24·1	5	0
September, 1901	37·3	37·3	37·5	37·6	123·0	113·5	23·9	24·1	7	0
October, 1901	37·4	37·2	37·5	37·2	122·6	110·8	24·3	26·0	4	0
December, 1901	37·5	37·3	37·5	37·3	128·0	112·0	22·8	23·3	0	0
January, 1902	37·5	37·4	37·5	37·4	123·0	106·8	23·6	22·8	0	0
February, 1902	37·4	37·4	37·5	37·4	122·7	104·4	23·7	21·7	0	17

The sole-reflex is normal, no ataxia, no sensory disturbances. Standing and walking are undisturbed. Major psychic deviations are absent, memory is slightly weakened.

The fits still show the same character as before the operation.

As will be seen from this brief account, this boy presents no striking deviations except his fits and the swollen veins on the left of his chest. When the pulse of this patient is felt, however, it is found to be small, regular, equal, with little tension and frequent, the radial artery being strongly contracted. Especially remarkable in this pulse is its frequency. Table I. refers to this. In the fifth and sixth columns are indicated under (M) the frequency of the pulse in the morning, under (N) at night. The numbers in these columns were obtained by taking the mean of an interval, indicated at the beginning of each

TABLE II.

March 6, 1902.	Pulse.	Respiration.
2.25 p.m.	103-104	24-26
2.30 p.m. Pressure upon both cicatrices during 12·6 sec.	109	25
2.35 p.m. Pressure upon both cicatrices during 17·5 sec.	110	24
2.40 p.m. Pressure during 16 sec.	116	24
2.42 p.m.	108	25
2.52 p.m.	103	24

horizontal line. The pulse was counted very accurately every day by the superintendent or first attendant of the ward. The table shows that the frequency of the pulse which at first, when the patient entered the ward, varied between 80 and 100 a minute, rose at once after the operation, while it had risen considerably when the boy came back for the third time. During the last months it varied between about 110 and 120 a minute. A careful and repeated examination of the heart fails this time also to reveal any deviation of it. Simultaneous pressure on both the cicatrices always effects a slight acceleration of the pulse, as will be seen from an observation recorded in Table II. During sleep the frequency of the pulse falls to its normal, as appears from an observation recorded in Table III.

The same phenomenon shows the respiration; at first about 20, it shows an increase to 26 a minute, falling off again to about 22 a minute during the first two months of 1902. Although this respiration frequency is above the normal and has gradually risen, it is not so manifest that this rise has been directly consequent on the operation. Also the numbers of the

respiration frequency are means of daily observations. Thirdly, Table I. shows that the temperature, which was normal at the outset, has slowly and steadily, though somewhat irregularly, risen. The mean temperature, derived from daily observations, varied in January and February, 1902, between 37·4° and 37·5° centigrade, and is very probably not to be considered as normal when compared with the temperature before the operation. A careful and repeated examination of the lungs and abdominal organs, as far as this is possible, shows no deviations.

On account of the mentioned facts it seems to us very probable that in man a cardiomotor and a respiration-accelerating

TABLE III.

July, 1901.	Pulse. M.	Pulse. N.	Pulse. At night during sleep.
10 ..	132 ..	116 ..	68-72
11 ..	104 ..	128 ..	80
12 ..	120 ..	108 ..	80
13 ..	120 ..	116 ..	72
14 ..	116 ..	116 ..	76
15 ..	132 ..	116 ..	72
16 ..	120 ..	112 ..	76
17 ..	100 ..	124 ..	80
18 ..	120 ..	124 ..	64

centre are found at the base of the medial frontal gyrus near the place where this borders on the anterior central gyrus.

The localisation of the two functions on the base of the second frontal convolution, in the immediate vicinity of the region where Horsley and others localise conjugate movements of the head, and of the eyes, gives us an explanation of some observations made by us in cases of hysteria.

Historia morbi, No. 128.—A. v. W., aged 17 years, girl, with typical hysterical fits, clavus, a feeling of a tie round the front, concentric reduction of the field of vision, with inversion of the limit for red and blue, rapid fatigue with increasing restriction of the field of vision. Points of tenderness in the lumbo-sacral part of the spinal cord, in the infra-mammary region on the right, in the ovarian region on both sides. Hemi-hypalgesia on the right. Both legs of this patient are contractured in the equinovarous position with feeble reflexes probably owing to the contracture, the big toes in hyper-extension. When walking there is a strong hysterical ataxia, which disappeared almost entirely, and in a short time, by regular exercise as well as the contracture in the limbs.

While recording pulse and respiration of this patient, an attack set in. Pulse and respiration are regular, and number 70 and 17 a minute. Next the pulse begins to show a slight acceleration up to 74, respiration showing slight irregularities and increasing in frequency to 19 (fig. 3A.).

Directly after these symptoms a sigh is heaved, respiration becomes more rapid and irregular, the pulse rising to 80 a minute. A few moments afterwards the attack commences, at first with inspiratory position of the thorax, followed by deepening and very considerable acceleration (fig. 3B.). Almost simultaneously the attack spreads over the face, the arms and legs. In this observation which is one out of a large number, we see the hysterical fit set in with acceleration of the pulse, inspiratory position of the thorax, and next with considerable acceleration and deepening of respiration. The onset of the attack shows, therefore, a syndrome which agrees with the anatomical relations which we suspected. This observation is corroborated by another in which the attack does not spread further, and appears exclusively as a respiratory access.

Historia morbi, No. 340.—Patient, J. H., descends from a neurotic family, the mother being hysterical, while in the father a psychosis, of which the definition is somewhat uncertain, is in progress of development. Patient is in dress, behaviour, and appearance a hysteric, and very liable to suggestion. She presents globus, clavus, restriction of the field of vision, anæsthesia of the pharynx, hysterogenic spots in the supra- and infra-mammary regions, on the left mastoid process, and in both ovarian regions, hemi-hypalgesia, anæsthesia *en manchette* affecting the arms and both legs. The attacks mostly begin with paræsthetical sensations and a slight contracture round the corners of the mouth. These symptoms may sometimes last for hours, but generally the attack begins soon afterwards with inspiratory tonus, sometimes attended with closing of the vocal cords, immediately followed by maximum inspirations and expirations with rotatory movements of the head round its vertical axis. The deep, very much accelerated respirations took place in the same tempo as the rotatory movements of the head; at first six every second, they soon grew a little less rapid. Such an attack sometimes lasted for hours with undisturbed consciousness. Further spreading of the attack did not occur. Fig. 4 gives the tracing of such an attack. Data about the frequency of the pulse of this patient we unfortunately do not possess.

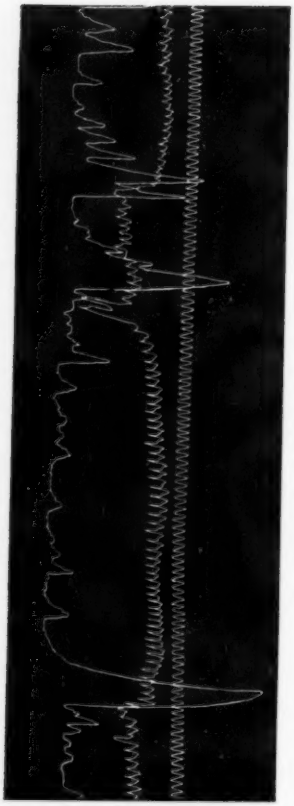


Fig. 1.

Fig. 2.

Fig. 3A

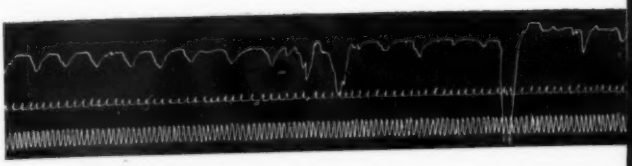


Fig. 4.

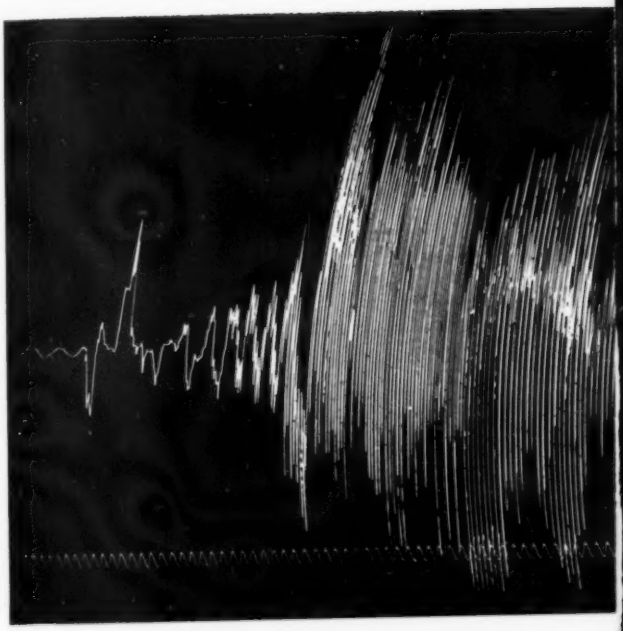


Fig. 5.

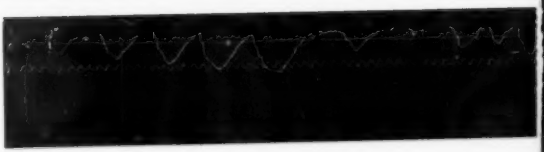
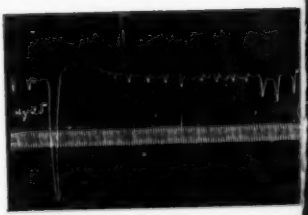


Fig. 6.



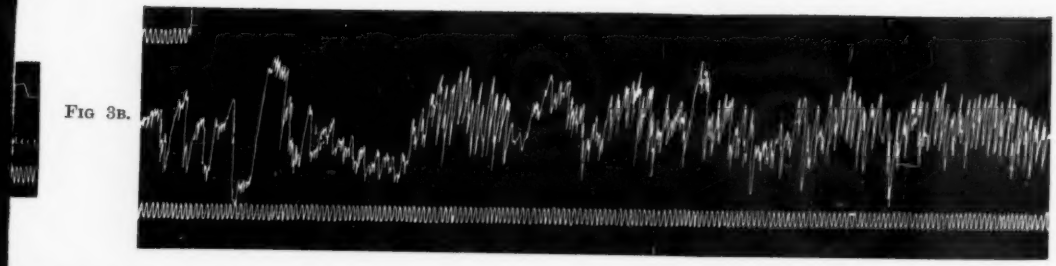
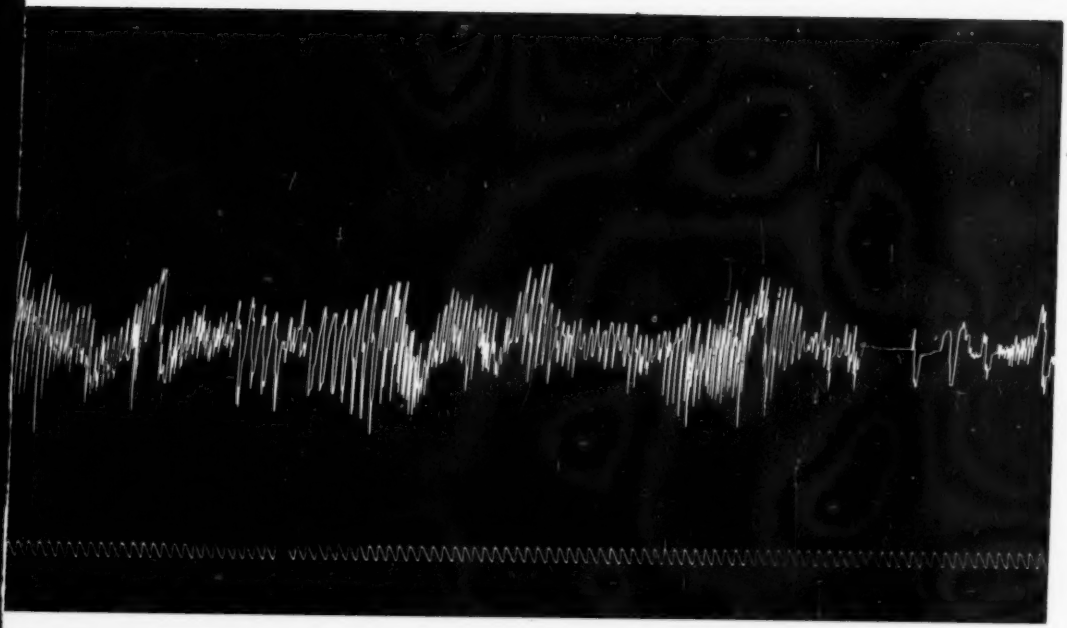
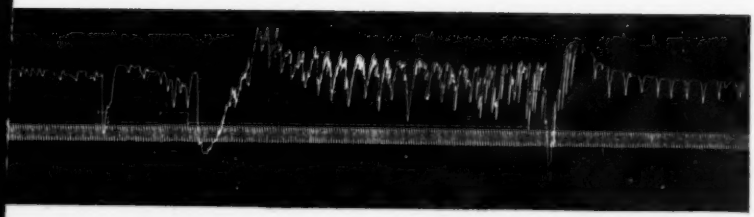


FIG 3B.





On account of the great influence which exercise in many cases has on hysterical patients, we caused our patients with respiratory attacks to learn how to fix their attention on their own respiration and to sigh very regularly and deeply.[1] At first this took place at command and assisted by periodic pressure on the thorax, later spontaneously at the moment when they felt an attack come on. Fig. 5 represents a curve in which a threatening attack, indicated by accelerated inspiration and growing irregularity of respiration, is suppressed by deep sighs. This curve was taken from the last of the patients described, who ultimately learnt in this way to suppress her attacks herself.

Starting from an entirely different point of view, Raymond and Janet[2] arrived at a similar treatment, when they found that concentration of attention was the only and effectual means to cause in one of their patients a respiration presenting the Cheyne-Stokes type to revert to a regular type.

In the course of our experimental investigations we have repeatedly succeeded, generally by over-stimulation of the cortical field which we described, in provoking respiratory attacks in the dog. These attacks remained restricted to the respiratory muscles, and so are completely comparable with the attacks shown by our last patient. For comparison we reproduce a curve (fig. 7) representing part of such an attack. We are quite aware that by the representation of facts here given we place part of the hysterical attack on a line with the epileptic attack, only the cortical field over which the extension takes place is a different one, at least in the beginning. The great number of transitorial types which are observed between both forms of attacks seems to us to justify this. On the other hand, we are also aware, however, that cortical extension alone cannot explain the hysterical attack.

[1] Beyerman, "Hysterie en Ademhaling," *Geneeskundige Bladen*, No. vii., 1901.

[2] F. Raymond and P. Janet, "Un cas du rythme de Cheyne-Stokes dans l'Hystérie."

ON THE PATHOLOGY AND BACTERIOLOGY OF LANDRY'S PARALYSIS.

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THE following paper was read at a meeting of the Neurological Society on April 2, 1903, and comprises :—

(1) A brief, critical review of our present knowledge of the pathology and bacteriology of Landry's paralysis.

(2) The record of an investigation of a fatal case of the disease, including :—(*a*) the isolation from the blood of a micrococcus which does not conform with any previously-described organism; (*b*) its discovery in the dura mater of the patient; and (*c*) the result of its inoculation into rabbits.

To the above has been added, in the form of an appendix, a more detailed description of the micro-organism and of the experimental part of the investigation.

I do not propose, to-night, to do more than touch upon the discussion which has arisen as to what is really meant by the term "Landry's Paralysis"; what cases should and what cases should not be included under that term; and what are the particular clinical symptoms and pathological findings which justify its use.

The confusion of ideas on these points may, in my opinion, be ascribed to three principal reasons; in the first place, the name was brought into use at a time when histological methods were not as advanced as they are at the present day, and more especially before the introduction of the Marchi and Nissl methods of staining nervous structures;

in the second place, it has only slowly become recognised that a disease, which was first of all regarded as invariably fatal, may sometimes take a more favourable course; and in the third place, even some of the recent numerous writers on the subject have failed to point out that both the clinical and pathological manifestations of what is generally admitted to be an infective or toxic process must necessarily vary in accordance with the length of its duration, and the virulence of the poison at work. Enough stress has not been laid upon the relative duration of symptoms when comparing the symptomatology and morbid anatomy of one case with another.

Death ensues in this disease when the muscles of respiration cease to meet the requirements of life, and depends, therefore, upon the incidence of the morbid process, upon certain parts of the nervous system, and, again, upon the intensity of its influence on those parts. Thus the fatal issue may be brought about by a rapid and intense affection of the spinal and bulbar centres within a few hours or days of the onset of symptoms, or, on the other hand, it may be considerably postponed or averted when the poison is less active in its effects.

It is not unreasonable to assume that if it were possible to examine microscopically the same case of Landry's paralysis at intervals of a few days, the results might be found to approximate very closely to many of those which have been described in the large number of cases now collected in medical literature. At an early period in the course of a case of moderate severity, we could imagine that a condition of marked motor palsy, with absent reflexes, no electrical changes and slight paræsthesiæ, would reveal, *post-mortem*, no abnormalities which could be demonstrated even by osmic acid or Nissl methods of staining in any part of the nervous system. A little later, more advanced motor and sensory disturbances accompanied by slight electrical and trophic changes might find their counterpart in early degeneration of both motor and sensory neurones, and in commencing chromatolytic changes in certain ganglion cells. Again, a few days and we should expect both the clinical

and histological evidences of the disease to be more marked, the additional phenomena of sphincter trouble and early muscular atrophy on the one hand being counterbalanced by the presence of advanced cell changes in the central nervous system, and an extension of the degenerative process to muscle fibres on the other.

Such a picture or series of pictures must necessarily be modified by what we know of the varying susceptibility to the action of particular poisons presented by different neurones, and also by the varying degree of virulence displayed by the same organism, supposing Landry's paralysis to be a specific disease, or by different organisms if it is capable of being produced by more than one member of the bacterial world. At the same time it must be admitted that the anatomical changes are sometimes inadequate to explain the cessation of functional activity, and we must look forward to more precise methods of examination to make clear this discrepancy.

A study of the now extensive literature on this subject assures one, at any rate, that the imaginary progression of events which I have just sketched is not without some basis of probability, and if we look for a moment at the cases which have occurred within the last few years, and which have been subjected to a careful and complete *post-mortem* examination by recent methods, we find examples of all the three conditions I have referred to.

The cases in which no pathological changes are to be found have become remarkably few, but Giraudeau (1) and Levi record an instance in a patient who displayed the clinical picture of the disease in an acute form, and who died ten days after the onset of symptoms.

Among the cases which exhibit definite *post-mortem* evidence of disease, a certain number have been only remarkable for the signs of degeneration in the peripheral nerves, and, on account of the absence or scarcity of cell changes in the cord, have been held to prove the peripheral origin of the disease. A majority of recent cases however, have shown significant changes in the nerve-cells of the cord, and especially in those of the anterior horns, and this

condition has often been associated with early myelin degeneration both in the peripheral nerves and in the white matter of the central nervous system. The intensity of the process as it affects the cellular elements has been of all degrees, and has varied from a condition which could hardly be regarded as abnormal to one which has closely resembled an acute anterior poliomyelitis.

The anterior roots have shown Marchi degeneration more frequently than the posterior roots, but in the latter, and even in the posterior ganglion cells, changes have also been described.

The most constant of all changes has been the marked vascular engorgement both in the cord itself and in the leptomeninges, and this hyperæmia has been accompanied in some instances by minute capillary hæmorrhages, and in others by an exudation of small round cells into the walls of the vessels and into the perivascular spaces. This last condition of cell infiltration is more remarkable, however, for its absence than for its presence in the class of case to which I am now referring.

This list comprises the morbid findings of modern times in a majority of the cases of Landry's paralysis, but there is a smaller group of cases in which the pathological process is much more severe, and amounts to a diffuse but intense inflammation of the cord and its meninges. It is characterised by engorgement of the vessels in the meninges and cord, by well-marked round cell infiltration of the vessel walls and perivascular spaces, and by the presence of areas of softening, sometimes limited to the gray matter and often to the anterior horn region. This condition may be found after a very short duration of illness and, although it is frequently associated with the clinical course of Landry's paralysis, really belongs pathologically to the category of meningo-myelitis. In a few members of this group bacteria have been demonstrated in the substance of the cord.

In order to complete a very brief summary of what we know of the morbid anatomy of this disease it is only necessary to add that in a few isolated cases hyaline degeneration of the vessel walls, thickening of the intima resembling

endarteritis syphilitica, and one or two other conditions have been placed on record, but cannot be said to possess great significance in view of their rarity.

Apart from the neuro-muscular system, only two morbid conditions are met with sufficiently often to justify their mention—enlargement of the spleen and evidence of extensive pleurisy in the form of old or recent adhesions; the frequency of the latter is quite remarkable, even when its prevalence in all autopsies is taken into consideration.

Experimental evidence is afforded by the work of many investigators, that all the pathological changes described in my first group of cases can be produced by circulating microbic toxins, even in the absence of the microbes themselves from the tissues, and this fact justifies one in thinking that in a particular case in which more or less of these changes are found, the condition is in all probability due to some intoxication, and this in spite of the fact that bacteriological examination may have proved negative.

This conclusion has been arrived at by many modern writers on the subject, and notably by American observers who have contributed largely to our knowledge of the disease, but there is an inclination on the part of some to assume that the toxic action is limited either to the spinal cord or to the lower motor neurons, or even by others to the peripheral nerves. In my opinion such views are too narrow, and I would regard the intoxication as affecting all parts of the central and peripheral nervous system, but with an intensity which varies with the susceptibility of the different neurons to the poison, and with the energy and duration of its activity

Assuming, then, that Landry's paralysis is a species of acute intoxication of the nervous system, the following questions arise :—

(1) Is it a specific disease due to one micro-organism?

(2) If there is a specific micro-organism, can the same symptom-complex be also produced by other organisms, such as the bacillus of influenza or of typhoid fever, by the gonococcus, &c., acting vicariously?

(3) Is the same condition capable of being brought about

by some poisons or poison, the result of disordered metabolism, as has been suggested by an abnormal state of the urine in a case related by Worcester (2)? In other words, is it ever the sign of an auto-intoxication?

The fact that these questions can be put and, in the present state of our knowledge, cannot be answered, is a practical admission that Landry's paralysis is at present to us only a symptom-complex and not a disease. We must look, therefore, to bacteriology to answer these questions and to put into some sort of scientific order a group of cases which are in clinical and pathological confusion.

During the last few years a considerable number of investigations have been made with a view to discovering a microbic origin for the disease, but the majority of these investigations have produced negative results, many of them have been incomplete and therefore unsatisfactory, and some of those in which bacteria have been found belong to my second pathological group and are, in fact, cases of meningomyelitis.

If we compare the cases in which some sort of bacterial examination has been made and has proved negative, with those in which positive results have been obtained, one or two interesting facts present themselves.

There are, as far as my researches have discovered, twenty-five members of the first class, *i.e.*, in which bacteria were looked for and not found either by cultivation or by staining tissues or by both methods. With very few exceptions, there was no *etiological* factor to be obtained in any member of this class, although influenza is mentioned several times as preceding the development of symptoms. "Influenza" used in this way is a well-abused term, generally referring to a febrile disturbance accompanied by pains in the back and limbs, and can hardly be looked upon as a scientific datum. The *pathology* of this class comprises the changes which I have described above as being capable of production by microbic toxins in the absence of microbes, and need not be detailed again.

The second class includes thirteen cases, some of which deserve more detailed notice.

In Centanni's (3) case, he found numerous bacilli in the peripheral nerves associated with interstitial neuritis, some meningitis and degeneration of the peripheral zone of the spinal cord; the author describes the case as a "neuromycosis."

In Eisenlohr's (4) case, the palsy came on in a patient suffering from pulmonary tuberculosis and two varieties of staphylococci were cultivated from the nerves, spleen and other organs. Areas of softening were found in the cord and the case appeared to be one of general infection by a common organism occurring in a patient whose resistance was lowered by another infective process.

Burghart's (5) case also died of pulmonary tubercle, and a streptococcus was cultivated from the blood.

Friedländer and Giese (6) describe a case of staphylococcic pyæmia in which the symptoms of acute ascending paralysis supervened. The organism was cultivated from an abscess.

In the patient described by Mouravieff and Montourine (7) there was no *post-mortem* examination, but the staphylococcus albus was found in the blood during life.

In a case of variola recorded by Oettinger and Marinesco (8) there supervened symptoms of ascending paralysis, and cocci were found in the sections of a softened cord.

In 1876 Baumgarten (9) found bacilli in the lungs, spleen, spinal cord and blood of a patient who had the clinical symptoms of Landry's paralysis.

Remlinger (10) in the case of a malarial patient who had an acute attack of ascending paralysis, found a few streptococci in sections from the spinal cord and succeeded in growing the same organism in pure culture from the same part. Inoculations into rabbits proved negative.

Marie and Marinesco (11) describe bacteria resembling anthrax bacilli and a diplo-bacterium in the cord of a case in which softening of the anterior horns was found *post mortem*.

Curshmann (12) discovered what he believed to be typhoid bacilli in the cord of a patient suffering from enteric fever who presented symptoms of a rapidly-spreading palsy.

Not one of these nine cases can be said to throw much light on the etiology of Landry's paralysis, and are interesting only because they seem to show :—

(1) That many of the common pathogenic organisms can, especially in patients debilitated by disease, give rise to symptoms of acute ascending paralysis and can produce changes in the cord and nerves resembling those which are found in cases of Landry's paralysis.

(2) That the organism of a specific disease such as enteric fever may sometimes invade the spinal cord, and produce clinically an ascending paralysis, and pathologically a diffuse or disseminated myelitis.

The following records are more interesting and more suggestive :—

(1) Courmont and Bonne (13) describe a case of Landry's paralysis in which microscopical changes were present in the form of chromatolysis of ganglion cells and fine diffuse Marchi degeneration of the myelin in the white columns. The blood of the patient during life proved sterile. From the cerebro-spinal fluid and from the cord was grown a diplococcic organism which was sometimes seen in chains, and which retained its colour by Gram's method. The authors considered that, although bearing certain resemblances to the meningococcus of Weichselbaum and to the pneumococcus, it probably belonged to the streptococcic group. Inoculations into rabbits a month after its isolation proved negative.

(2) Piccinino (14) found oval cocci in groups and small chains in the vessels, perivascular spaces and cells of the cord. The micrococcus was said to resemble the diplococcus of Weichselbaum, but no cultures were made. The pathological changes in this case were of the nature of anterior horn cell degeneration.

(3) Roger and Josué (15) have recorded a case of acute ascending paralysis, without any known etiological factor, in which they found Nissl changes in the lumbar enlargement. Sections stained for bacteria did not demonstrate the presence of any organism, but cultivations from the heart blood produced a growth of a diplococcus resembling the

pneumococcus. Injections of this coccus into a mouse did not prove fatal. A rabbit submitted to the same experiment died at the end of twenty-one days with symptoms of paraplegia, and the diplococcus was recovered from its blood.

(4) Another diplococcus similar in some respects both to the organism described by Weichselbaum, and to that described by Still was found by Dr. Risien Russell (16) in a case of ascending meningo-myelitis under Dr. Buzzard at the National Hospital.

(5) Although they have, perhaps, only an indirect bearing on the subject of this paper, it is worth while to record briefly the results of an investigation into an epidemic form of ascending paralysis among the inmates of a lunatic asylum, undertaken by Chantemesse and Raymond (17). The paralysis in these patients was preceded by vomiting and œdema, and was followed by rapid muscular atrophy. The morbid anatomy consisted of degenerative changes in the peripheral nerves and in the ganglion cells of the cord, with some vascular lesions. Cultures from the cerebro-spinal fluid and from various organs revealed the presence of a bacillus resembling in some particulars the proteus of Hauser. Inoculated into rabbits, it produced symptoms of ascending paralysis and a condition, *post mortem*, of meningo-myelitis. Inoculations of the toxins *without* living baccilli produced, also, a fatal ascending paralysis with œdema and congestion of the gray matter of the cord and degenerative changes in the ganglion cells. These cases bore a strong resemblance to beri-beri of the East and cannot be considered as an example of an epidemic form of ordinary Landry's paralysis.

These last experimental results are analogous to those obtained by other observers such as Claude (18) with snake poisons, and Moltchanoff (19) with the gonococcus toxin. The latter found chromatolytic changes in the anterior horn cells, and later in the cells of the posterior root ganglia, besides diffuse degeneration in the white columns of the cord and in the peripheral nerves of the animals into which the toxins were injected.

The conclusions I deduct from this summary of our

present knowledge of the pathology and bacteriology of Landry's paralysis are briefly the following:—

(*a*) Even by modern histological methods a few cases present no demonstrable lesions.

(*b*) In the large majority of cases the lesions are such as can be produced in the central and peripheral nervous system by the action of microbic toxins apart from the microbes themselves. In these cases it is the rule to find that bacteriological investigations have given negative results.

(*c*) In a few cases the lesions are those of a disseminated or diffuse myelitis or meningo-myelitis of varying degrees of intensity, and in some of these pathogenic organisms have been demonstrated in the meninges, spinal cord, and cerebro-spinal fluid, and occasionally in the blood and other organs as well.

In other words it has been shown by investigations on man and the lower animals that the clinical manifestations of Landry's paralysis are the result of either a local infection, a general pyæmia, or lastly, and most frequently, of an acute intoxication.

It is in the hope that they may throw some light on the obscurity of these intoxications that I bring before you my observations on a case which I shall now record.

Before doing so I would express my gratitude to Sir William Gowers for his permission to make use of the notes of the patient who was under his care in the National Hospital, and for some valuable suggestions he made with regard to the investigation.

G. L., a man 33 years old, was admitted into hospital on December 20, 1902, and the clinical notes from which I quote were taken by the house physician, Dr. Stanley Barnes.

The patient had had syphilis fifteen years previously, and since 14 years of age had followed the occupation of a printer, which had recently necessitated his working in close proximity to a hot stove and standing on a hot floor.

Fourteen days before his admission he had noticed "pins and needles," numbness, and burning in his upper and lower

extremities. Stiffness and heaviness in his hands and feet supervened three days later and prevented him from continuing his work. The signs of paresis spread up the extremities from the peripheral to the proximal muscles, and he became unable to walk four days before he came under observation. For several days he had also suffered from shortness of breath and some difficulty in swallowing.

On examination the man was found to be thin and pale, cheerful, placid, and perfectly intelligent. His special senses and cranial nerves appeared to be healthy, but he had distinct paresis of his neck muscles. Respiration was embarrassed when he talked, and was purely costal in type, the diaphragm being absolutely paralysed. All trunk muscles were very weak. The legs and arms were markedly paralysed, and the proximal muscles seemed to have suffered more severely than the peripheral in all four extremities. There was no muscular atrophy, and no diminution to electrical excitability.

The subjective paræsthesiæ mentioned above were present, but objective sensation was perfect, except for a slight blunting to touch below the knees.

All deep and superficial reflexes were absent, and the sphincters acted normally.

The paralytic phenomena became more marked, especially in relation to respiration, and the patient died four days later. The temperature varied between 99° and 100°, and the pulse between 100 and 130. The duration of his symptoms extended over eighteen days.

At the autopsy, which was performed early in the afternoon of the day on which he died, I found rigor mortis present, and noticed a rather unusual lack of moisture in most of the tissues. The cranium, vertebral column, and soft meninges appeared healthy; the dura mater I will refer to later. The brain and spinal cord were noticeable for nothing except their marked vascularity, and both were firm in consistence and free from any suggestion of softening.

The central nervous system together with pieces of several peripheral nerves and spinal ganglia, and a few pieces of muscle were put aside to harden in 10 per cent. formalin.

The heart, liver and kidneys were healthy in appearance; the spleen was full-blooded and moderately large and firm. The right lung was adherent to the parietes over its entire surface, but beyond some hypostatic congestion showed no sign of disease. The left lung had some slight adhesions at the apex, but presented no evidence of old or recent tubercle.

At the beginning of the autopsy I inoculated various culture media with material from the cerebro-spinal fluid, spinal cord, blood and spleen with all due precautions, and also prepared film specimens from some of the same tissues. The culture tubes together with sterile pipettes containing an additional supply of heart's blood and cerebro-spinal fluid were handed over at once to Dr. Eastes, from whose report I shall quote later.

Histology.

Portions of the spinal cord, spinal ganglia, peripheral nerves and muscles were removed from the formalin after forty-eight hours, and examined by the following staining methods, sections being embedded and cut in gum, paraffin and celloidin:—Weigert-Pal, Marchi (using Busch's fluid), Nissl (using thionin and methylene blue), Van Giesson, and hæmatoxylin and eosin; for bacteria, methylene blue, carbol-thionin, carbol-fuchsin, and Gram's stain were also made use of.

The results of my examination must be summarised for the sake of brevity without much further reference to the technique employed.

The vessels of the pia-arachnoid and of the cord were all dilated and filled with blood; in some sections the red corpuscles had escaped from the capillaries and had formed minute scattered hæmorrhages. The vessel walls showed no evidence of disease. Every now and then a slight round cell exudation about a vessel was come across, but this condition was distinctly exceptional. A few vessels seemed to contain a greater quantity of leucocytes than is usual, but as a rule the normal proportion of red and white cells was maintained.

The pia mater and the connective tissue elements of the cord showed no change; here and there the sub-pial tissue had the appearance of being the seat of some proliferation.

No myelin change was detected by the Weigert-Pal method, but sections stained in Busch's fluid from all parts of the cord presented a large number of black dots scattered indiscriminately throughout the white columns. These dots, under high powers, appeared to represent droplets of altered myelin, some within the myelin sheaths and some lying between contiguous fibres. Parts of the peripheral zone of the cord were the seat of more intense black staining by this method. Most of the ganglion cells of the cord were deeply stained by the osmic acid.

The axis cylinders in the cord and roots were unusually well stained by logwood, and were possibly slightly swollen; this condition has been pointed out to me by Dr. Batten and Dr. Collier as frequently present in toxic processes.

The ganglion cells of the anterior and posterior horns, and of Clarke's column presented in the large majority of cases a normal condition as regards their nuclei and their chromatin granules, but a certain number, and in my opinion more than is the rule in healthy cords, showed various degrees of chromatolysis and excentration of nuclei. This opinion was arrived at from the examination of a large number of sections, and has reference to the lumbar enlargement in particular, where many of the cells appeared to be unduly swollen.

Except for vascular engorgement and the presence of rather an unusual number of so-called "mast-cells," the spinal root ganglia presented no remarkable features.

The peripheral nerves (sciatic, ulnar, and external popliteal) stained by Busch's fluid resembled the white matter of the cord in being the seat of numerous small scattered drops staining black with the osmic acid; by other methods the only noticeable condition was the number of mast-cells, many of which had burst and dispersed their basophilic granules in the connective tissue around them.

The muscles examined showed no abnormal features by the logwood methods, but treated by osmic acid presented

undoubted evidence of an early degeneration affecting a large number of the fibres. In transverse sections the gray-staining fibres, interspersed among the healthy ones, gave a most striking and unusual appearance to the preparations.

The obvious deduction to be made from this account of my microscopical examination is that the morbid changes were very slight in degree of intensity, rather widely distributed, toxic in character, and, finally, of such a kind that they might easily have escaped detection by the older methods of staining.

Bacteriological.

Before recording the bacteriological results of this inquiry I should like to express my thanks to Dr. Eastes for the time and skill he expended on the cultivation of the micrococcus which was found, and for the benefit of his valuable opinion in the study of its characteristics.

The tubes inoculated at the autopsy were incubated at 38° C.; the material in the pipettes was inoculated into broth and on to the surface of blood serum and agar, and incubated aërobically at the same temperature. Inoculations from the same source were made on to glucose-formate broth and incubated anaërobically.

All the tubes inoculated with blood from the spleen and with cerebro-spinal fluid remained sterile, though kept under observation for fourteen days.

The solid media and the glucose-formate broth inoculated with the heart blood remained sterile.

In the broth tube inoculated direct from the heart blood, and in another tube of broth inoculated with the blood received in the pipette, after a week's incubation under aërobic conditions a slight flocculent deposit was observed, which proved to consist of a micrococcus.

The growth in the two tubes was sub-cultivated on blood-agar, glycerine-agar, broth, glucose-peptone, blood serum, and milk.

By the end of another week growth had occurred in sub-culture in broth, and on one of the tubes of blood-agar. On

the surface of the latter there were two kinds of colonies, the only macroscopic difference between them being that of size. Each proved to consist of a micrococcus resembling that found in the original cultures, though the cocci in the smaller colony proved to be more uniform in size than those in the larger colony, which were distinctly pleomorphic. This micrococcus occurred usually in cultures as a diplococcus of about the same size as the gonococcus, though in its pleomorphic condition many of the cocci were much larger and others were smaller than the gonococcus. The organism stained moderately well with methylene blue, but did not retain Gram's stain.[1] It was remarked that the large cocci, which may perhaps be regarded as involution forms, stained somewhat irregularly, portions of the coccus taking up the methylene blue with avidity.

The smaller colonies contained cocci which, besides being more uniform in size, were less frequently diplococcic and more equally stained than those in the large colonies.

Each half of a diplococcus was hemispherical in shape, and the opposed surfaces were distinctly flattened. Occasionally two diplococci lying close together formed a tetragenous group.

The blood-agar tube was filled up with broth and re-incubated for six days, by which time a flocculent growth was apparent. This tube was handed over to Dr. Eyre, who was kind enough to do some inoculation experiments on rabbits for me. I shall refer to these experiments when I have detailed the results of my bacteriological examination of the human tissues.

Sections of the cord from different levels, sections of the spinal ganglia, and sections of the peripheral nerves were stained by Löffler's methylene blue, and by carbol-thionin, and carefully searched, but no definite bacteria could be found. Portions of the pia-arachnoid were stained in the same way, spread out and examined with the same result. Smears from the heart blood only showed the presence of one or two doubtful organisms. The spleen and kidney

[1] In sub-cultivated specimens the coccus *did* retain Gram's stain fairly well; see Appendix.

substance also proved negative as far as bacteria were concerned.

As a result of my experience with one of the inoculated rabbits, I determined to examine the soft vascular tissue which lies on the outer side of the spinal dura. This tissue in my case appeared to be more œdematous and much more engorged with blood than did the same tissue in patients who died from a different cause. It was found impossible to remove the thin vascular membrane on the surface without taking a portion of the fibrous structure underlying it at the same time, and only a few pieces out of a large number of attempts were thin enough to stain and examine under a high power. In all of these the vessels were seen to be choked with red corpuscles, and in parts the blood had escaped into the surrounding tissue. Many of the specimens proved negative as regards the presence of bacteria but in a few there were areas in which minute cocci were present in large numbers. The cocci were generally to be seen in close proximity to capillary vessels, sometimes lying free and almost in the walls of the vessels, sometimes lying within cells at a little distance, and sometimes appearing in conglomerate clusters in which it was difficult to distinguish the individual cocci. In consequence of the thickness of the preparations in which the cocci were suspended, the individual members of one group often lay in different planes, and the morphological characters of the organism were very difficult to make out except by careful focussing with high powers; a diplococcic appearance, similar to that of the micrococcus cultured from the blood, was every now and then to be distinguished. There was less variability in size, and the usual diameter was a trifle smaller than that of the majority of the cocci in the smaller culture colonies. The examination of this dural tissue was otherwise only remarkable for the presence of a moderate leucocytal reaction, and for the presence of numerous mast-cells of unusual size. The majority of these appeared to be bursting with granules, and many had burst, with the result that the scattered granules were at times rather difficult to distinguish from the micro-organisms. The points of difference

were, however, definite enough, the granules being as a rule smaller, more spherical, always staining redder with methylene blue than the bacteria, and never to be found within the tissue cells.

Experimental.

I now come to the experimental inoculations; for the carrying out of these I was fortunate enough to secure the services of Dr. Eyre, Bacteriologist to Guy's Hospital, to whom I am deeply indebted for the trouble he took in the matter.

The material employed for injection into rabbits was obtained from the blood-agar culture of the coccus derived from the heart blood of the patient, and revivified by filling up the tube with nutrient broth, and incubating at 37° C. for nine days. The broth was uniformly turbid, and on microscopical examination showed the presence of cocci in pairs and short chains, but the majority in tetrads.

Rabbit "A" received ·5 cc. of the turbid broth intravenously on February 2, but remained unaffected until March 4, when it was killed and revealed nothing *post-mortem*.

On the same day Rabbit "B" received ·5 cc. of the turbid broth in the subdural space through the frontal bone (anæsthetic A.C.E.); a few hours after inoculation, the breathing became stertorous, and the animal remained in a condition of stupor for two hours, when the respiration again became normal and the rabbit commenced to take food. The wound healed by first intention and the animal seemed to be unaffected until February 9, when some weakness of the hind limbs was noticed. On February 12, all four limbs were found to be paralysed, but the animal continued to feed well. On February 14, I examined the rabbit carefully, and noted as follows:—

Respiration is rapid, diaphragm acting; trunk muscles are probably weak. Left hind limb, moderate strength and knee-jerk obtained; right hind limb is very weak, flaccid, and the knee-jerk is absent. Both fore limbs are very weak, the right weaker than the left. The animal cannot stand,

and generally lies on its right side with the right limb under the left.

On February 23, the rabbit's condition remained the same, and it was killed. The heart blood was examined microscopically with negative results; cultures taken from the same source immediately also proved negative. Some of the heart blood was aspirated into a sterile pipette and incubated at 37° C. for seventy-two hours. The experimental inoculations performed with this reinforced blood proved negative as far as they have gone. Cultivations were made from the reinforced blood upon various media. Some of the blood-agar tubes and one of the broth showed scanty growth at the end of nine days; as this did not increase, the tubes were filled up with serum broth and again incubated. The growth which had resulted by March 20 was removed and carefully centrifugalised, and the deposit used for microscopical examination and for further inoculation, which has, up to the present time, given negative results. The organism in this deposit was very pleomorphic, and took Gram's stain better than previous specimens had done.

The only positive result was therefore obtained in Rabbit "B," in which a non-fatal general paralysis supervened a week after the inoculation, and was accompanied by no signs of interference with the natural functions or general health of the animal.

I removed the central nervous system and a portion of one sciatic nerve of the rabbit within two hours of its death, and placed them in 10 per cent. formalin solution. In doing so it was observed that the wound produced at the site of inoculation had healed perfectly without suppuration, and that the brain presented no evidence of injury beyond a minute red spot no larger than a pin's head and situated some distance in front of the motor region.

The *technique* followed in examining the histological appearances of the nervous structures and meninges was practically identical with that employed in the case of the human subject, and the results which were obtained will only be briefly summarised.

(1) Marked engorgement of the vessels of the meninges and of the cord.

(2) Punctate hæmorrhages here and there into the substance of the latter.

(3) A few patches of leucocytal infiltration in parts of the pia-arachnoid, but little or none around the smaller vessels within the nervous tissues.

(4) Diffuse Marchi degeneration in the white matter of the cord, and especially in the peripheral zone.

(5) A few degenerated fibres in the sciatic nerve.

(6) Complete absence of organisms from the cord and leptomeninges.

(7) Only a few sections were stained by Nissl's method, and I found no definite cell changes in those which I examined.

The dura mater of the rabbit is sufficiently thin and transparent to allow of its being stained and spread on a glass slide for examination.

With the methylene blue stain, and less clearly with Gram's method, a micrococcus was found in abundance in many parts of it, and was seen to take a similar position in regard to the vessels to that taken by the coccus in the same tissue in man. The microscopic appearance of the tissue differed from that seen in the human theca by reason of the entire absence of any mast-cells, but resembled it in the small amount of leucocytal reaction. The micrococcus was often diplococcic, sometimes tetragenous, and appeared to be similar in size and shape to the organism observed in the case of Landry's paralysis, but it was less frequently found within the tissue cells. I was able to satisfy myself that the cocci were situated nearer the external than the internal surface of the dura; that is to say, in the more vascular part of the membrane.

———

Put shortly, the results of the investigation are as follows:—

(1) A micrococcus was isolated in pure culture from the blood of a patient who died of Landry's paralysis.

(2) An organism, indistinguishable from that which was cultivated, was found in large numbers in the external part of the spinal dura of the same patient.

(3) A subdural injection of the cultivated coccus into a rabbit produced after some days a rapidly-spreading palsy.

(4) The same organism was discovered in the dura mater of the rabbit and isolated in pure culture from its blood.

(5) The changes in the nervous system in both the patient and the rabbit were of the kind produced by toxins, and in neither case was the microbe to be demonstrated in the nervous structures themselves or in the pia-arachnoid.

The slow and scanty growth of the organism in the primary cultures from the blood of both the man and the rabbit, its absence from the blood smears which were examined and from the interior of vessels seen in sections, lead me to infer that this micrococcus is not to be found in abundance in the blood; in other words, the condition of neither the man nor the rabbit was a true blood-infection.

The sterility of the cerebro-spinal fluid in the case of the man, and the absence of the organism from the lepto-meninges in the man *and* the rabbit, points to the conclusion that the cerebro-spinal fluid is not the favoured medium for its growth.

The fact that, although introduced sub-durally into the rabbit, the organism was found only in the external layers of the spinal theca is in harmony with the view that it was carried from the former situation to the latter by the cerebro-spinal fluid and this suggestion is supported by the investigations of the late Dr. George Elder (20) and of Professor Leonard Hill (21). Dr. Elder injected small quantities of Prussian blue sub-durally and traced the granules into the perivascular and other lymph spaces of the theca where it was taken up by the endothelial cells. Dr. Hill concludes from his own observations that "the pathway of the filtration of the fluid from the cranial cavity may be through the Paccionian bodies, *through the dura*, or through the veins of the pia mater."

The question at once suggests itself:—Does the lodgment of the organism in the perivascular spaces and cells of the theca merely represent a terminal stage in the combat of the tissues with the organism, and did the actual growth of the coccus take place in the cerebro-spinal fluid at an

earlier date? The other alternative appears to be that the organism reached this tissue either through the blood or through the cerebro-spinal fluid and there found the conditions necessary for its growth and multiplication. I am inclined to favour the latter alternative for two reasons; in the first place no cocci were to be seen in the leptomeninges where one would have expected to find them, if they had flourished in the cerebro-spinal fluid; in the second place the appearance of the coccus in pairs and tetrads in the dura suggests active life in that tissue. On the other hand some of the preparations seem to show that the organisms in the theca had seen their best days by the way in which they had been taken up by the cells and sometimes collected into shapeless clusters. This evidence, if it is evidence, of a short life is certainly in harmony with what we know of the clinical course of the disease, the victims of Landry's paralysis usually dying within the first three weeks of the onset of symptoms or recovering altogether.

The answer to these questions must be left until further researches have been made, but I cannot help thinking that some light might be thrown on the matter if the dura mater were the subject of more careful investigation in the future, not only in cases of ascending paralysis, but also in other diseases of the nervous system which are undoubtedly, or probably, of microbic origin.

The mode of entry of the micrococcus into the system of the patient is a subject on which I feel quite unprepared to offer any suggestions.

The question of the identity or non-identity of the organism in my case with better-known organisms, and notably with those which are associated with the names of Weichselbaum, Still, and Risien Russell, is one which cannot be definitely decided at the present time; nevertheless, it must be stated that although it has certain morphological resemblances to the two former it differs materially from all three in its staining and cultural characteristics.

If, for purposes of identification or reference, the organism described in this paper deserves a name, its predilection for the spinal dura mater naturally suggests the term "micrococcus thecalis" as its proper designation.

Bale & Danielsson, Ltd., Lith.

In conclusion, I do not claim that my investigation proves that all, or even many cases of Landry's paralysis are due to this organism, but I venture to hope that it may, if confirmed by other observations, help to expose a hiding-place from which members of the bacterial community have been wont, unknown to us, to exert their pernicious influence on the delicate structures of the central and peripheral nervous system.

Description of Figures in Plate.

Fig. 1.—This represents the micrococcus as seen in films made from one of the larger colonies on blood agar. Note the extreme pleomorphic character of the growth.

Fig. 2.—The same from one of the smaller colonies. Magnified in both about 1,000.

Fig. 3.—This is a drawing of a small portion of the spinal theca in Rabbit "B." Magnified about 1,000. Stained by Löffler's methylene blue.

Fig. 4.—Three small portions taken from different parts of the theca in the patient G. L. The same magnification and stain as in the other figures 1, 2, and 3. Two mast-cells are represented with some detached granules.

Note.—Microscopic specimens showing these conditions and also the pathological findings in the cord, peripheral nerves, and muscles were exhibited at the meeting of the Neurological Society, at which the paper was read.

Appendix.

A.—(Chiefly from Dr. Eyre's report.)

The material employed for injection into rabbits was obtained from the blood-agar culture of the coccus derived from the heart blood of the patient, and revivified by filling up the tube with nutrient broth and incubating at 37° C. for nine days.

The broth was uniformly turbid, and on microscopical examination showed the presence of cocci, some in pairs and short chains, but the majority tetrads; all, however, stained but feebly with the ordinary aniline dyes, and only partially retained the stain when treated by Gram's method. Subsequent cultures showed marked irregularity in size of cocci, similar variations in arrangement, and, finally, that the coccus stained by Gram.[1] Sub-cultivations upon agar,

[1] The technique employed was: anilin gentian violet for three minutes, wash; Lugol's iodine until film ceases to become appreciably blacker, wash: absolute alcohol until no more colour is discharged, and alcohol runs off colourless.

glycerine-agar, blood-agar, blood serum, and in nutrient broth, incubated at 37° C., remained sterile at the end of seven days.

Inoculation Experiments.

Rabbit "A."—Weight, 1,800 grams, received on February 2, 0·5 cc. of the turbid broth intravenously (posterior auricular). The animal remained unaffected until March 4, when it was killed. *Post-mortem* examination, *nil.*

Rabbit "B."—Weight, 3,320 grams, received on the same day 0·5 cc. of the turbid broth in the subdural space, introduced through a trephine wound in the frontal bone (anæsthetic A.C.E.). A few hours after inoculation the breathing became stertorous, and the animal remained in a condition of stupor some two hours, when the breathing again became normal, and the rabbit commenced to take food. The wound healed by first intention, and the animal appeared to be unaffected until February 9, when some weakness of the hind limbs was noticed. On February 11 the right hind leg was completely paralysed, and on the following day all four limbs were found to be paralysed. The animal, however, continued to feed well.

On February 23 the rabbit was killed.

Post mortem: (1) Central nervous system, examination by E. F. B., see p. 111; (2) heart blood examined microscopically, result negative; heart blood examined by cultivations, result negative.

About 3 cc. of the heart blood was aspirated into a sterile pipette, and the point sealed off in the flame. The pipette was placed in the incubator at 37° C. for seventy-two hours. At the end of this time:—

(*a*) Inoculation experiments were made with the reinforced blood.

Rabbit "C."—Received 0·5 cc., reinforced blood intravenously. The animal was never visibly affected. On March 24, that is, four weeks after inoculation, the animal was killed. *Post-mortem* examination, *nil.*

Rabbit "D."—Received 0·5 cc., reinforced blood under

the dura mater, through a trephine wound as in Rabbit "B." The animal was apparently unaffected, the wound healing rapidly and well. On March 19 about 5 mg. centrifugalised deposit from serum broth culture (*vide* Rabbit "E") emulsified with 0·5 cc. broth was introduced into the cranial cavity through the original scar. The animal still appeared to be unaffected. It was killed March 30. *Post-mortem* examination:—No changes in the central or peripheral nervous system. A considerable number of the same micrococci were found in the dura mater as in Rabbit "B."

(*b*) Cultivations were made upon various media and incubated at 37° C. Some of the blood-agar tubes and one of the broth showed scanty growth at the end of nine days, but as the growth had not visibly increased four days later the tubes were filled up with serum broth and again incubated. The scanty growth which had resulted by March 20 was removed from each tube and carefully centrifugalised, and the deposit used for microscopical examinations and for inoculation.

Rabbit "E."—This animal received about 5 mg. of the centrifugalised deposit emulsified in 0·5 cc. broth under the *dura mater*, as in Rabbits "B" and "D." The rabbit remained unaffected, and *post mortem* showed no changes and no cocci.

B.—The following is a brief summary of the characteristics of the organism as far as they have been ascertained:—

Cultural.—Growth took place at 37° C. only on blood agar and in broth, and only aërobically. The growth was never apparent until seven or more days after the inoculation of the tubes, and it took the form of large and small greyish-white colonies on blood agar. After a few days growth ceased and the organism died quickly.

Morphological.—In cultures the coccus was generally diplococcic, each diplococcus having the appearance of a split pea; frequently they were grouped as tetrads, or as sarcinæ. They exhibited very marked differences in size, some of the cocci being quite three times the size of others. In the smaller colonies the cocci were less often diplo-

coccic and more uniform in size than in the larger colonies. In the tissues of both the man and the rabbit the organism exhibited the same morphological characters, except that they were less pleomorphic. They were frequently intracellular. They were never encapsulated or lanceolate.

Staining.—In cultures the cocci took the aniline dyes indifferently well, and often unequally. Specimens taken from the primary cultures did not retain any colour by Gram's method, but those taken from sub-cultures, and from cultures derived from the blood of the rabbit, were partially or completely stained by that method. The cocci in the human and the rabbit's theca were stained well by methylene blue, and in the latter they were coloured by Gram. The human theca was not stained by Gram.

Experimental.—The primary cultures proved pathogenic to a rabbit when introduced subdurally, but not when inoculated intravenously. Secondary cultures from the rabbit appeared to have lost their virulence.

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A CASE OF TUMOUR OF THE AXIS ILLUSTRATING THE FUNCTIONS OF THE THIRD CERVICAL SPINAL SEGMENT.

BY WILLIAM THORBURN, F.R.C.S.,
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AND
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Burnley.

THE following case came under the observation of one of us (Dr. Gardner) at the end of June, 1901, and was transferred to the Manchester Royal Infirmary shortly afterwards. For the general account of the history and symptoms we are jointly responsible; for that of the operation and subsequent course, as well as for the remarks which follow, Mr. Thorburn is alone responsible.

History.—J. S., blacksmith, began to suffer in 1897, when 51 years of age, from pain about the left shoulder, which, in the course of the following twelve months, gradually extended to the left side of the neck, and especially involved the region of the occiput. The pain grew steadily worse, and was for a long time markedly periodic, awakening him from sleep about one o'clock each morning. Towards the end of 1900 the neck became somewhat stiff, and from that time onwards pain was experienced on moving the head. Shortly afterwards cramps began to be felt in both legs, and a little weakness was noticed in the left arm. In the spring of 1901 there ensued a sensation of great coldness in the left side of the neck and left upper limb, with tingling sensation in the left hand, while the pain diminished and the weakness increased. The left upper limb now became almost totally paralysed, and paralysis rapidly followed in the left lower limb, tingling sensations and some shooting pain in each case preceding the loss of power. Very shortly afterwards the right lower limb was also paralysed. In April, 1901, the left arm and forearm

were useless, but some power of movement remained in the muscles of the hand. In May the left upper limb was completely paralysed, the lower limb of the same side was "almost useless," and the right lower limb "very clumsy." Shortly after this date tingling sensations came on in the right hand, and were followed by loss of sensation and gradually increasing weakness in that limb also. (On another occasion the patient stated with greater probability that the right arm became paralysed before the right leg.) The lower limbs were now completely paralysed and liable to attacks of intense spasm. At the end of June, 1901, a feeling of fulness was experienced in the chest, and it was noticed by friends that when talking the patient had to stop from time to time in order to take breath.

Symptoms.—On July 5, 1901, J. S. was seen by both of us, and three days later he was admitted to Mr. Thorburn's wards in the Manchester Infirmary. Careful notes were taken on both of these occasions, but they may be combined into one general description.

The patient was very grey, worn, emaciated, and appeared to be considerably more than 55 years of age. He was paraplegic and anæsthetic below the neck. Mentally, he showed marked dulness and hebetude, with occasional rambling. At the back of the neck there appeared to be slight fulness on the left side immediately below the occiput; the second cervical spinous process was markedly prominent and its environment distinctly tender; there was no difficulty in supporting the head, but the neck was held rigidly fixed.

The main subjective symptom was a constant sensation of choking and of "burning in the chest." The left upper limb was completely paralysed and flaccid, while no reflexes could be obtained; its fellow was wasted and almost completely paralysed, but retained a little power in the biceps and in the flexors of the fingers and wrist; reflexes were obtained from the triceps and wrist tendons and appeared to be exaggerated. The lower limbs were paralysed and rigid, while they were occasionally drawn up by spasm; the muscles were not greatly wasted and were extremely irritable; knee-jerks were most active, and both ankle clonus and Babinski's reflex were well defined. The abdominal walls were quite flaccid, and diaphragmatic respiration could not be detected. No movement was observed in the intercostal muscles. The trapezius and sterno-mastoid muscles acted vigorously in respiration, those of the left side being, however, considerably smaller than those of the right. So far as could be

seen respiration was entirely dependent upon these muscles; the number of respirations was about 28 per minute; at each breath the chest was drawn upwards like a solid unexpanding mass, and the abdomen was rendered rather more tense thereby; speech was naturally greatly impaired. A distinguished neurologist seeing the breathing remarked: "If you had told me a man could go on living like that I should not have believed you." There was no control over the rectum, and urine dribbled constantly away. The muscles of the face and tongue were unaffected, as were those of the eyeballs; both pupils were small, but on the left side the pupil and the palpebral fissure were distinctly smaller than on the right. The cranial nerves presented no abnormality.

The sensory disturbances were difficult to investigate on account of the mental dulness, but the following facts were ascertained with certainty. From the prominent and tender second cervical process, a narrow strip ran round the left side of the neck, gradually widening and occupying the area from the hyoid bone to the chin in which there was very marked hyperalgesia; over this area slight scratching, and even stroking, was very clearly felt, and somewhat painful. Beneath this area there was rapid transition to complete anæsthesia to all stimuli; it was not practicable to draw an absolutely sharp line of demarcation, there being a margin about half an inch wide running from immediately below the second cervical spine to the hyoid in which there was occasionally anæsthesia, but below this margin sensation was lost. The complete anæsthesia extended downwards to about the level of the clavicle and acromian process, but then began to diminish in intensity, so that over the trunk and limbs both touch and pain could be everywhere recognised, and localisation of sensation was fairly good. On the right side of the body the limbs and trunk were nowhere completely anæsthetic, and below the clavicles there did not appear to be any difference between the two sides of the body. Above the right clavicle, sensation improved by a very gradual margin on passing up the neck, and there was no hyperæsthesia upon this side. Sensation was perfectly normal on the face, ears and vertex of both sides, but no accurate examination could be made of the occipital region, as attempts to sit up caused pain sufficient to distract the attention, while respiratory embarrassment equally prevented examination in any but the dorsal position. From such examination as we could make under these circumstances, we came to the conclusion that sensation was unaltered over the whole head, and

that all sensory symptoms ceased on the left side above the hyperæsthetic band already described, and on the right side above a fading margin somewhere about the middle of the neck. The condition is represented in the following diagrams :—

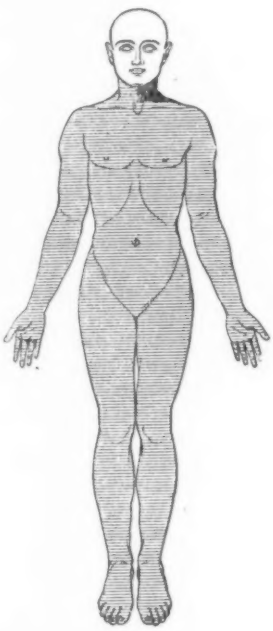

FIG. 1.

Showing areas of complete and partial anæsthesia.

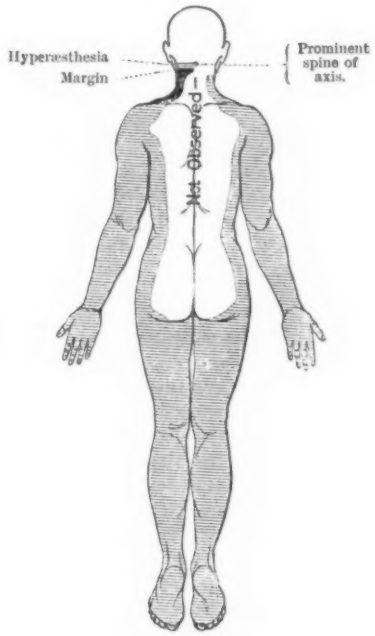

FIG. 2.

Showing complete and partial anæsthesia and posterior portion of hyperæsthetic band.

No "trophic" changes were present, but on July 5 and July 8, the left arm was very œdematous, and the right less markedly so; on July 8 when the man arrived at the infirmary this condition had completely disappeared.

During the interval between July 5 and July 8, the general condition had become much worse, and on the 9th and 10th of the month he showed further rapid deterioration; respiration was increasingly difficult, and the mental condition had become much

confused; on the evening of July 10 fever appeared for the first time, the temperature rising to 100°. On July 11 he became still worse; presenting continuous rambling and active delirium throughout the night; temperature *mane* 97·6, *vesp.* 99·6.

Operation.—The operation had been arranged for the morning of July 12, but the man was then almost *in articulo mortis*; his feeble respirations were at the rate of 28 per minute, and he was in a condition of continuous muttering delirium. It was only after much hesitation and consultation with Dr. Gardner and Mr. Alexander Wilson, anæsthetist to the Infirmary, that I decided

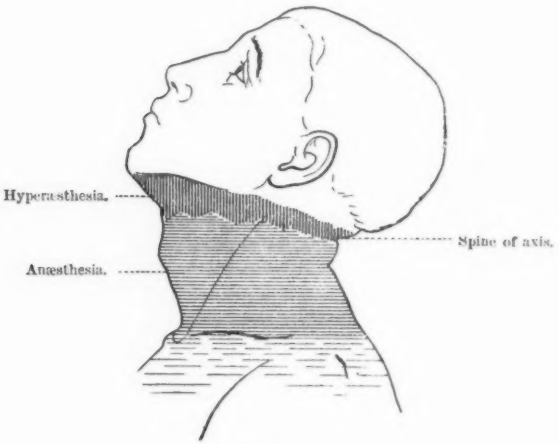

FIG. 3.

Showing detail of hyperæsthetic band and upper margin of anæsthesia on left side.

to proceed under such desperate circumstances with an operation which seemed not unlikely to prove immediately fatal.

The patient was taken to the theatre and carefully supported upon the right side. Chloroform was administered by Mr. Wilson. A median incision about 5 in. long was made over the occiput and upper part of the neck, the muscles being retracted by sutures. The laminæ of the second and third cervical vertebræ were readily exposed, cleared, cut through upon both sides with bone forceps, and removed. It was at once obvious that the theca was

pushed backward against these laminæ, and Mr. Wilson was of opinon that respiration was immediately relieved by their removal. A soft round encapsuled mass about the size of a hazel nut, was now exposed lying in front and to the left of the theca vertebralis and attached to the body of the second cervical vertebra; it was not adherent to the dura mater which was easily separated and held lightly to the right by a raspatory. Enucleation of the intact tumour was impossible, and it had to be removed in fragments by means of a scoop and Volkmann's spoon; it extended deeply into the second cervical vertebra, occupying a rounded cavity large enough to contain the end of the index finger. So far as could be ascertained the soft, almost gelatinoid, mass was completely encapsuled within the bone, and it appeared to have been entirely removed. The roots of the spinal nerves did not appear to have been compressed, and the theca, which was not opened, was now free from pressure. Breathing being now unquestionably much easier and deeper, the wound was closed by muscle sutures and skin sutures. Bleeding gave little trouble, and the vertebral artery was not seen. After application of the dressing, the head and neck were supported in a felt case. Wound healing was uneventful, and the sutures were removed on July 21. The scrapings of the tumour were examined for me by Dr. Melland, who regarded them as probably a myxo-sarcoma.

The following notes of the subsequent progress of events were taken by my house surgeon, Mr. Telford:—

July 12.—Immediately after operation respiration was much improved; there was distinct bilateral chest movement; respiration rate fell from 28 to 16; pulse 100, fairly good. Treatment.—Oxygen inhalations, and strychnine administered hypodermically.

July 13.—Improvement maintained; resp. 20; some expectoration; patient very drowsy, but comfortable; slight œdema of left hand and arm. (This symptom has not been present since July 8.)

July 14.—Much improved; respiration 21; marked return of power in right upper limb; up to this point temperature rising to about 100° at night with nocturnal delirium.

July 15.—Improvement maintained; fair power in right arm and leg; slight movements of left leg which had not been previously noticed; temperature normal; mental condition not so good—incessant rambling and delusions of people about the bed. *Vesp.*—Quantity of urine diminished and slight hæmaturia; no distension of bladder (catheter not used at any time).

July 16.—Patient more rational; distinct movements of left

foot; right arm and leg as before; left arm still quite paralysed; temperature normal.

July 18.—Condition of limbs unaltered; respiration easier; expectoration diminished and less foul. *Vesp.*—More marked delirium and shouting all night. Temperature again raised (100°).

July 19.—General condition feebler.

July 21.—Sutures removed from healed wound. After this time the temperature remained normal to the close of life. Delirium less marked and strength greater. Paralysis as before.

July 22.—Right arm possesses considerable power and right leg actively moved; left arm still completely paralysed, but no longer œdematous; better sensation in both right limbs. Respiration easy (18) with good chest expansion.

July 23.—Right arm sufficiently recovered to enable patient to remove dressings, bedclothes, &c.; very noisy and delirious.

July 25.—Motor and sensory power still improving, but general condition not so good.

July 30.—Right upper limb appears to have complete power, but there is no inclination to use the hand for feeding, &c. Right lower limb moved with considerable force. Slight movements only in left foot. Left upper limb *in statu quo*. The mental condition renders accurate examination of sensation impossible, but there is little if any anæsthesia on right side of body; on left side sensation is dull throughout and localisation very imperfect. Shooting pains in left limbs.

August 6.—Slight movement of left upper limb. General condition bad and bedsores tending to form over sacrum and scapulæ.

August 13.—Movements of head and limbs slowly increasing in power. Flexion and extension of left elbow practicable, but associated with pain.

From this time onwards there was gradual sinking; bedsores formed rapidly at all points of pressure; the pulse was always rapid and feeble. Temperature remained normal. Delirium was almost continuous, but paralysis and anæsthesia still appeared to improve, chest movements were better and as late as September 12 movements began to be noted in the left hand. On September 15 the man died exhausted.

Autopsy.—For the *post-mortem* examination and a report as to the nature of the growth I am indebted to Dr. Rothwell, but I deeply regret that death occurred during my absence from Manchester, and that the spinal cord was lost by an assistant in the pathological department. Bedsores were present over the occiput, sacrum and spines and angles of the scapulæ; over the sacrum

was a large necrotic area extending down to the spine. The aorta showed a few small patches of atheroma. The left pleura presented numerous fairly firm adhesions. In the left lung near the lower part of its anterior border was an abscess about the size of a tangerine orange. The body of the second cervical vertebra was occupied by a growth situated mainly to the left of the middle line, and about the size of a walnut. Posteriorly this projected slightly into the spinal canal, in front it extended to the muscular aponeurosis and laterally it was bounded by osseous tissue. It had no connection with and was not pressing upon the theca. Structurally it was a round-celled sarcoma containing many large ovoid cells resembling those of cartilage and with a hyaline matrix.

The general outlines of the above case are sufficiently well defined. We have a sarcoma of somewhat complicated histological structure arising in the body of the axis, growing very slowly over a period of at least four years, projecting into the spinal cord, and then forming a nodule or button which never became adherent to the dura mater, but which severely compressed the theca and cord, especially upon the left side between the second and third cervical vertebræ.

The diagnosis was made with precision by Dr. Gardner, and was sufficiently obvious at the time when I first saw the patient, but I wish now particularly to refer to certain points in connection with the operation and the symptoms. My justification for so doing lies in the rarity of such cases, and in the fact that early death usually prevents examination of symptoms in pressure lesions above the fourth cervical root, while no operation had previously been recorded at this level of the spinal cord. A careful search has since enabled me to find the record of only one similar case, which is so brief that I have quoted it *in extenso* at the end of this paper.

The *operation* itself is of interest from two or three points of view. The condition of the patient when it was carried out was most desperate, and the administration of an anæsthetic in itself appeared to be highly dangerous. In spite of this latter difficulty, it was not thought prac-

ticable to perform the vigorous and delicate manipulations of laminectomy under local anæsthesia alone. Again laminectomy for any condition is comparatively rarely called for or performed at so high a level, and I am not aware of any published cases except that quoted below, while I have personally only once before removed the arch of the axis. The operation, however, presented no difficulties, and from this, and one other case in which I have removed the arch of the axis, I should say that if the deep muscles of the neck be thoroughly withdrawn from the vertebræ, laminectomy in the upper cervical region can be performed with unusual ease and speed. In both of my cases I have carried the incision well on to the occiput, so as to obtain ample room. In the present instance the muscles were easily separated to the left side by retractors, but in the other case to which I have referred a transverse incision was made to one side of the upper end of the vertical cut, and the muscles were separated from their insertions on that side. The laminæ having been fully exposed by one or other of these methods and cleared by the raspatory can quite readily be cut across by bone forceps, and it is unnecessary to use the saw, which would be somewhat difficult to manipulate in so deep a wound.

The results of the operation in the present case, although disappointing, are not without encouragement for the future. The nervous symptoms at once began to improve, and the improvement was steady and progressive until interfered with by the increasing general cachexia. As the *post-mortem* examination showed that the growth had hardly re-entered the vertebral canal, and as the cord was quite free from pressure, it is clear that death was not due to any irreparable injury of the cord itself, but to the deterioration of the general health which had preceded the operation. Apart, therefore, from the question of malignancy, an earlier operation would almost certainly have been successful.

The *motor symptoms* here met with present no special points of interest, and paralysis of these segments is observed in many cases of progressive muscular atrophy, syringo-myelia and the like; the marked wasting of the

left sterno-mastoid and trapezius and the affection of the left eye simply indicate the intensity of the injury and emphasize the extent to which the left motor nuclei must have been paralysed, while the retention of some power in the right arm and the intact condition of the right sterno-mastoid and trapezius indicated that the right side was less injured. It is therefore probable that the left phrenic nerve alone was completely paralysed.

Upon the profound respiratory paralysis we have already dwelt. It is not suggested that respiration was effected solely by the sterno-mastoids and trapezii, and it is probable that the diaphragm continued to act slightly, but it was quite impossible to detect any movement other than those described.

The *level of the anæsthesia* upon the left side is here of the greatest interest as illustrating the upper border of the distribution of the third cervical root, a distribution not hitherto noted in pressure lesions.

Apart from the experimental work of Sherrington, the sensory areas supplied by each spinal segment or posterior root have been determined in man by three principal methods, viz., by anatomical dissection, by clinical observation of injuries and similar lesions of the spinal cord or its roots and by noting the distribution of herpes zoster and the associated degeneration of the root ganglia.

The purely anatomical method presents difficulties due to the impossibility of tracing nerve-fibres throughout their course, difficulties which render it practically useless for the investigation of segmental areas, although such data as can be obtained by this method possess the advantage of a certainty which attaches to no other.

The clinical study of injuries of the spinal cord and of its nerve roots with a view to the determination of their segmental distribution has received much attention since the earlier generalisations of Ross. The present writer published many observations some fifteen years ago, and these have since been extended by Starr, Bruns, Kocher, Wichmann and many others, but cases suitable for the purpose are comparatively rare and our knowledge is largely

due to scattered observations. Among these I know of no case demonstrating the affection of any segment higher than the fourth cervical.

The observations of Head, Mackenzie, and others, have given admirable clinical pictures of the distribution of herpes zoster at all levels, and have shown clearly that this disease indicates the distribution of the nerve-fibres of each root ganglion. The results do not, however, entirely coincide with those obtained by study of the segments of the spinal cord itself and it still remains an interesting and unsolved question whether the spinal segment and the posterior root ganglion exactly correspond to one another.

These various methods have now enabled us to define with great certainty the cutaneous distribution of many of the spinal segments, and we may take it as absolutely established that there is a territory supplied by the first four cervical roots and bounded above by the line of the vertex ear and chin (Scheitel-Ohr-Kinnlinie), and below by a line which runs across the front of the chest about the level of the second ribs, passes outwards below the acromion processes, and then gradually ascends towards the fifth, sixth or seventh cervical spinous process. The average extent of this great area supplied by the first four cervical nerves is fairly represented by the shaded portion of the annexed diagrams which are taken from the outlines of Seiffer ("Spinales Sensibilitätsschema," Berlin, 1901); figs. 4 and 5.

The crown-ear-chin line which separates the cervical plexus from the sensory territory of the fifth cranial nerve is also well shown in the following diagrams (fig. 6) modified from Seiffer, these and all other illustrations ignoring the auricular branch of the vagus of which we know nothing.

In this great area it is anatomically certain that the first cervical or sub-occipital nerve plays little, if any part, and it is equally certain that the great occipital branch of the second cervical nerve occupies the upper part of the area. It is further shown by many cases of injury and disease of the spinal cord that the fourth cervical segment supplies its lower portion, and on general morphological grounds

as well as from the general direction of fibres demonstrable by dissection, it is probable that the various roots lie roughly in their numerical order from above downwards. The more precise differentiation of the distribution of these roots remains to be demonstrated.

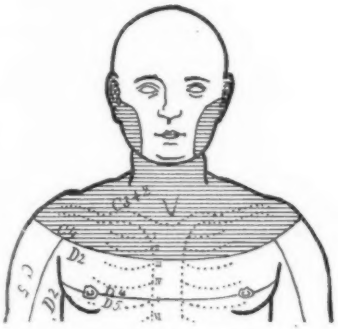

FIG. 4.

Showing shaded distribution of first four cervical nerves (Seiffer).

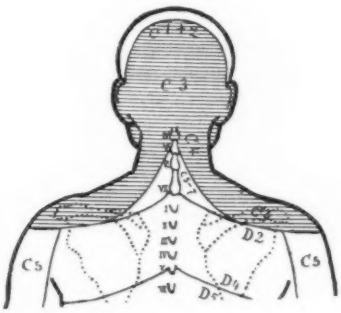

FIG. 5.

Showing shaded distribution of first four cervical nerves (Seiffer).

FIG. 6.

Showing upper margin of distribution of cervical roots at junction with trigeminal area (crown-ear-chin line). (Seiffer).

Turning now to the anatomical evidence as to the sensory distribution of the third cervical root, we find that its posterior primary division sends a small "third occipital" branch, which has a small distribution on the back and lower part of the occipital bone internally to the great

occipital, while other small branches ramify over the trapezius, but even in this short course the origin of the sensory filaments is confused by the union of branches which constitute the "posterior cervical plexus." The anterior primary division also unites with those of both the second and fourth root to form the cervical plexus, and it thus has an opportunity of contributing to the superficial cervical, great auricular, and small occipital nerves, or to the descending branches which run towards and over the shoulder girdle. We thus find what we may describe as its potential distribution over an area bounded above by a line running from beneath the occipital protuberance downwards and outwards to a point about midway between that bony prominence and the tip of the mastoid process, thence running up upon the side of the head behind the mastoid to a point well above the ear, and again downwards in front of the external ear and along the posterior border of the lower jaw to the middle line. So irregular an outline is, however, not characteristic of the usual arrangement of a sensory segment of the spinal cord, and it is clear that the territory thus defined is supplied also by the second cervical root. The lower boundary of the third cervical segment is equally not to be distinguished by anatomical methods from that of the fourth, but upon this point our present case throws no fresh light.

So far as I can ascertain this great doubtful territory has been subdivided only by Head's observations upon herpes zoster. Kocher (*Mittheilungen aus den Grenzgebieten der Medizin u. Chirurgie*, Jena, 1896), certainly gives three distinct areas which he assigns to the second, third and fourth nerves, and which are indicated in the following diagrams, figs. 7, 8 and 9, but he does not give any evidence in favour of their differentiation. Seiffer, who has very carefully studied the whole literature of this subject, draws no boundary lines but illustrates the *à priori* probabilities already referred to by the numerals shown in figs. 4 and 5.

Head (BRAIN, 1894, p. 339) in noting the areas of tenderness associated with certain visceral diseases, defines two areas which he calls the "sterno-mastoid" and the "sterno-

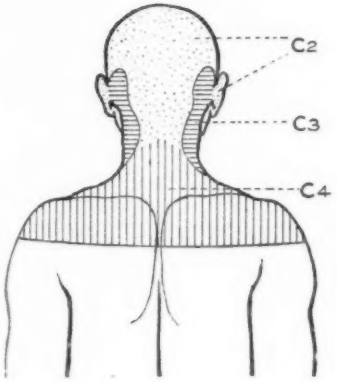

FIG. 7.

Showing areas supplied by second, third, and fourth cervical nerves (Kocher).

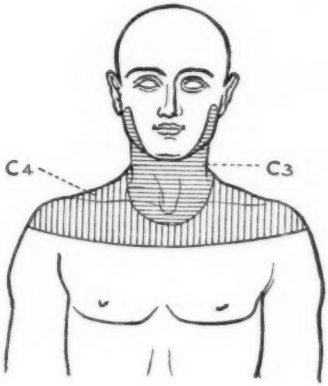

FIG. 8.

Showing areas supplied by second, third, and fourth cervical nerves (Kocher).

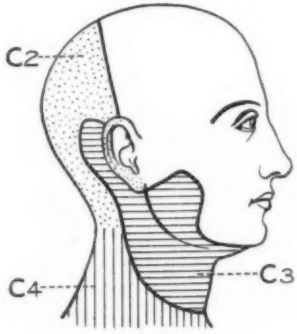

FIG. 9.

Showing areas supplied by second, third, and fourth cervical nerves (Kocher).

nuchal," and which on theoretical grounds, described in his paper, he regards as representing the territories of the third and fourth cervical segments. These areas are indicated in the annexed diagram from his plates, figs. 10, 11, 12 and 13:—

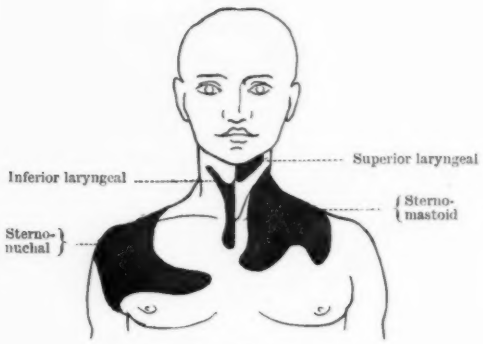

FIG. 10.

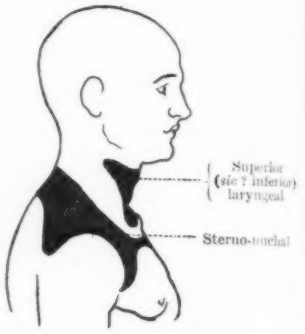

FIG. 11.

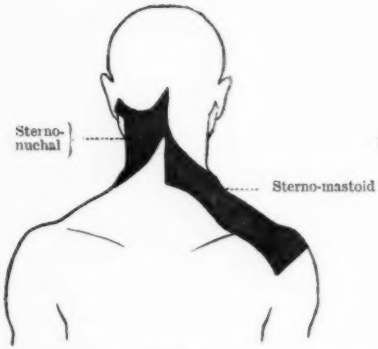

FIG. 12.

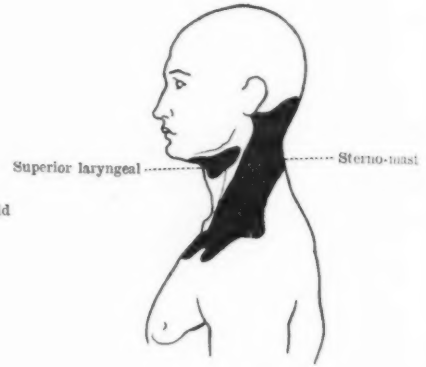

FIG. 13.

Head's cervical areas.

The evidence in the original paper that they are in any way connected with spinal segments appear to me to be insufficient but in a later article (BRAIN, 1900, p. 353) Head shows that herpes zoster is associated with disease of the ganglia of the posterior spinal nerve roots, and he illustrates several cases due to disease limited to the third and fourth cervical ganglia in which the distribution of the herpes corresponds closely with that indicated in his diagrams.

Evidence of this class is much more reliable than that derived from tenderness in association with visceral disease and Head's second paper appears to demonstrate with accuracy the distribution of fibres connected with the third and fourth cervical root ganglia.

There have, however, always been discrepancies between Head's areas and those determined by the anatomist, or by clinical observation of lesions of the spinal cord itself—discrepancies the cause of which still remain to be elucidated. It is for this reason that the case now recorded appears to be of importance, inasmuch as it probably represents the upper level of the sensory distribution of the third cervical segment, as determined by a lesion of the spinal cord itself. The operation did not indicate any pressure upon or traction of the roots, and, so far as could be ascertained during its somewhat hurried course, the medulla only was compromised by the growth. Assuming, therefore, that we have here a true picture of the anæsthesia produced by pressure upon the third segment of the cord, and comparing the area affected with that indicated by Head, we find that it comes further forward upon the neck and it includes his "inferior laryngeal," and at least a part of his "superior laryngeal" areas, as well as the "sterno-mastoid" region.

If this be an accurate representation we should thus be left with a complete differentiation of the third cervical sensory segment, and we may then on anatomical grounds exclude the first segment, and fill in the second as occupying the entire area from the upper boundary of the anæsthesia of our case to the crown-ear-chin line of the trigeminal, thus completing the localisation of the segmental distribution of the spinal nerves throughout the body.

It is on these grounds that I have thought the above record of importance. It is fully admitted that a single case, in which the difficulties of observation were considerable, must not be taken as establishing with certainty the generalisation which is here attempted. Such cases are, however, likely to remain few, and to present evanescent symptoms. Until we are provided with others we may

therefore place some reliance upon an observation which has in its favour the fact that it expresses the general band-like arrangement of the spinal segments, while it does not appear to be incompatible with any of the observations and deductions quoted above.

In conclusion, and to complete the scanty literature of neurology and surgery of tumours of this region, I have added the following brief report from the *New York Medical Record* of July, 1902, of the case described by Putnam and Krauss, and operated upon by Roswell Park. This record only came to my knowledge after the above notes had been written, but in its general aspects it presents a close similarity to that of Dr. Gardner.

"This was the report of a case by Drs. James W. Putnam and William C. Krauss, of Buffalo. The patient was a man 45 years of age. He had always been in good health, and gave no history of injury. Two years ago he had attacks of sharp pain in the back of the neck, radiating to the occiput. These increased in frequency, and were at times accompanied by vertigo. Later, numbness and weakness developed in both hands and arms. Then the legs became similarly affected, until he was unable to walk. Motion was entirely lost in the muscles of the left arm and leg. There was some power in all of the muscles of the right arm and right leg, and no muscular rigidity. All of the reflexes were highly exaggerated with the presence of patellar and ankle clonus and the Babinski reflex. There was loss of control over the bladder and rectum, with total loss of sensation on both sides from the clavicle down. The vision was good, and the pupils reacted readily to light. The diagnosis was made of tumour of the cervical portion of the cord, and operation was advised. This was done by Dr. Roswell Park, April 28, 1902, and a sarcoma involving the third cervical segment was found and removed. During the five weeks since the operation there had been some improvement, which still continued. The writers claimed this case to be unique for the following reasons: (1) It was the only tumour of the spinal cord affecting the upper cervical region which had been so far recorded; (2) it was

the only cervical cord tumour which had gone on an uninterrupted course toward recovery; (3) it was definitely located and quickly removed without sacrifice of spinous processes and laminæ, and the short incision closed with remarkable rapidity; (4) from the surgeon's standpoint it was located in the most inaccessible portion of the spinal cord, by virtue of the cervical curvature of the spinal column offering a concave field for operation instead of a convex field; (5) it was the only tumour of the cervical segment of the cord in which distinct phrenic nerve disturbances were noted."

After some discussion by the American Neurological Association, "Dr. J. W. Putnam, in closing, said that when the tumour was removed from the cord it showed that compression had been exerted upon the cord by a cup-like depression, which was on both sides of the median line. The delay before operation was due to the obstinacy of the family physician, who insisted that there was no tumour present, but that it was a case of hysteria. The patient was going on to incomplete recovery."

Reviews.

Die Physiologie und Pathologie der coordination eine analyse der Bewegungsstörungen bei der Erkrankungen des Centralnervensystems und Ihre rationelle Therapie. Von Dr. Otfrid Foerster, Assistant der Psychiatrischen Klinik der Universität, Breslau. With 63 figures in the text. (Jena, 1902, verlag von Gustav Fischer.)

For several years the author acted as assistant to Dr. Frenkel of Heiden, in which capacity he enjoyed exceptional opportunities of studying the subject upon which he writes. The book consists of two parts; the first deals with the physiology and pathology of coordination in general, while the second part, comprising the remaining three-fourths of the work (232 pages), is devoted to a consideration of the defects of coordination which are met with in tabes dorsalis. Dr. Foerster defines coordination as follows: "By coordination we understand the ability of the organism by means of its muscles to produce external effects which fulfil a definite purpose or a set task, accomplishing these effects with the smallest possible waste of energy."

After elaborating this definition the author proceeds to discuss certain questions concerning muscular synergism and the correlated action of antagonistic muscles. There is no constant preformed relation between the activity of muscles and their antagonists; the antagonists are stimulated to contract or not, as the case may be, according to the required effect, their intervention depending upon the momentary need at the time and occurring only during the production of the effect.

The correct choice of the degree of innervation necessary for an individual movement is sometimes very difficult and the organism makes use of the antagonists to control the movement with a greater degree of certainty, the coordinating activity or ability of the organism consisting in the choice of the necessary degree of innervation.

The sensory and motor theories of coordination are discussed at considerable length, as is the probable part taken by the spinal cord, cerebrum and cerbellum in coordinated movement.

To the pathology of coordination twenty pages are allotted. Disturbances of coordination are defined as "all those disturbances of motion which appear when an aimed-at effect of no matter what kind is produced." Compensation or "the reparation of a defect of one coordinating mechanism by another" is alluded to in this relation.

The second part of the book deals exhaustively with incoordination as met with in tabes. The author sums up a chapter in which the spinal, motor, sensory, and cerebral theories of tabetic ataxia are fully considered by stating that the ataxia depends on a disturbance of the afferent impressions, spinal, cerebral and cerebellar, which are necessary for coordination.

A short chapter on the method of describing tabetic disturbances of coordination is followed by a detailed description of the defects which occur at each individual joint, with frequent references to the rational method of treatment most suitable to meet the defective coordination. Numerous figures are introduced to illustrate points referred to in the text.

The author is to be congratulated on the production of a work which bears evidence of much original observation and is well worthy of study by those who are particularly interested in the question of the ataxia of tabes and its treatment by coordinated exercises.

EDWIN BRAMWELL.

Contribution a l'Etude de l'anatomie Pathologique de la Syringomyélie. Par Le Dr. L. BISCHOFSWERDER. (C. Naud, 3, Rue Racine, Paris. 1902.)

THE author of this paper, working in the laboratory of Dr. Pierre Marie, has examined pathologically, and describes in detail, two cases of syringomyelia. Not only have the spinal cords been investigated, but also the peripheral nerves and muscles. The lesion in the latter, consisting of degeneration of nerve-fibres and thickening of the connective tissue.

The author concludes that the nature of the lesion in syringomyelia is a chronic and progressive inflammation of the ependyma,

which causes either dilatation or obstruction of the central canal, according to the manner of growth of the tissue. He considers that the epithelium is capable of undergoing the transformation necessary to the formation of the gliomatous tissue. The cells lose their cubical or cylindrical shape, become elongated in a lateral direction, produce long filaments with a more or less modified nucleus in the centre, while the protoplasm becomes clear, transparent, and homogeneous. Another form of transformation of the epithelium is their alteration into peri-ependymal cells, the cells becoming so fused with the neuroglia cells that they are practically indistinguishable from them. The direct relation between these two elements is further demonstrated by the frequent proximity of the stratified epithelium with the peri-ependymal cells.

The lesion generally begins in the cervical region of the cord, and extends above and below along the walls of the central canal, and it is in the lumbar region that the changes are most recent and best studied.

The growth and the cavity formation of the gliomatous tissue are dependent on the condition of the vessels which are embryonic in type and derived from the peri-gliomatous zone. Although this is the usual method of formation, the author agrees that the condition may arise from a congenital hydromyelia. The path for the heat, cold, and pain sensation probably lies in the anterior gray and white commissure, since the almost complete destruction of the posterior gray commissure in the lower portion of the cord did not give rise to any symptoms in the corresponding portion of the body. The fibres for tactile sensation do not run in the gray matter, but remain in the posterior columns. The sausage-shaped fingers are not due to œdema, but to a fatty degeneration of the skin and to a vascular hyperplasia. No direct connection could be traced between the amount of trophic disturbance of the limb and the spinal lesion; and, although these trophic lesions are due to vaso-motor disturbances, it is impossible to localise centres for vaso-motor disturbances in the spinal cord.

FREDERICK E. BATTEN.

PROCEEDINGS OF THE NEUROLOGICAL SOCIETY OF THE UNITED KINGDOM.

At the Annual Meeting held at 11, Chandos Street, W., on Thursday, January 22, 1903, the Presidential Address was delivered by JOHN NEWPORT LANGLEY, M.A., D.Sc., F.R.S., on "The Autonomic Nervous System." (See page 1.)

AT the Clinical Meeting, held at 11, Chandos Street, on Thursday, February 26, 1903, at 8.30 p.m., the following cases of Myopathy were shown:—

The cases have, for sake of convenience, been classified under the following headings: (1) Facio-scapulo-humeral type (Landouzy-Dejerine); (2) Juvenile type (Erb); (3) Pseudo-hypertrophic type; (4) Infantile type; (5) Peroneal type; (6) Anomalous cases.

(1) Facio-scapulo-humeral Type (Landouzy-Déjérine).

Dr. W. L. ASCHERSON.—*Case of idiopathic muscular atrophy.*

Edith M., aged 21.

Family history.—No evidence of hereditary influence. One brother was in St. George's Hospital and was registered as suffering from "progressive muscular atrophy." He was aged 19, and his symptoms came on at the age of 15. A consideration of his notes suggest strongly that he was suffering from idiopathic muscular atrophy, but whether juvenile type of Erb, or facio-scapulo-humeral, is uncertain.

Personal history.—Symptoms began at age of 14. Weakness and deformity of shoulder-girdles first noticed. Face does not seem to have been noticed first, and as a child she did *not* sleep with the eyes open. Disease progressed down the arms to the hands. Patient has *not* noticed weakness of legs or gait. The

weakness was preceded by dull, aching pain. There is evidence of other neuroses. "Fits" when a child, and one recently (none have been seen). The girl also has compensated mitral regurgitation, and has had subacute rheumatism lately.

Present condition. Face.—Marked myopathic facies. The frontalis, orbicularis palpebrarum, zygomatici, orbicularis oris, are paretic. Electrically their response to galvanism and faradism is diminished. No R. D. or qualitative change. Both sides about equally affected.

Upper extremity.—Marked wasting of the muscles attached to the scapula, serrati, and trapezii more so than rhomboids. Scapulæ are winged with the lower angle tilted upwards, and inwards, the outer (humeral) angle being depressed by the weight of the arm, producing marked characteristic deformity. The infra-spinati have escaped and stand out prominently. Deltoids much affected. Of the arms, the biceps and triceps are affected. The supinator and longus seem to have escaped. The extensors of the wrist and the common extensors of the fingers are involved, but the extensor indicis and extensor minimi digita have escaped. The intrinsic muscles and interossei seem to have escaped, though the thenar and hypothenar muscles seem flattened. The extensors of the thumb, metacarpal and phalanges are involved, producing typical ape hand. The electrical reactions correspond, to a certain extent, with the affected muscles, and show diminution of reaction to both currents. Some of the muscles (supinator longus) which show no paresis or wasting show marked sluggishness of reaction to electricity. R. D. is nowhere found.

Lower extremity.—Glutei wasted, giving characteristic deformity (median prominence). There is marked lordosis and the gait is slightly waddling.

Flexors of the thigh are much weakened, particularly the left.

Extensors of the thigh only slightly affected.

Extensors of knee are affected, and patient cannot straighten the leg or the thigh. The knee-jerks are absent on both sides. The girth of the thighs is unequal (right is > left). The legs show no disparity in girth, and are little affected. Flexion of the foot on the leg is slightly impaired. Extension of the toes is imperfect and there is tendency to hyper-action of the interossei of one foot (claw foot). The peronei evert the foot perfectly and are not affected. Inversion of the foot is also good.

Electrical reactions.—As far as these have been tested there is diminished reaction to galvanisation in the quadriceps.

Trunk.—The diaphragm and intercostals are apparently unaffected. The latissimus dorsi is much paralysed and wasted on both sides. The intrinsic muscles of the spine seem to have escaped and stand out prominently.

Sensation is unimpaired throughout. There is NO *fibrillary* twitching.

Superficial reflexes normal.

Points of Special Interest:—

(1) Apparent late onset of facial atrophy.

(2) Presence of initial rheumatoid pains and other neuroses in the individual.

(3) Involvement of the common extensors of the fingers with escape of the special extensors of the index and little finger.

(4) Involvement of extensors of the thumb (a bilateral ape hand).

(5) Elevation of the outer canthus of the eye, causing Mongolian appearance. It is suggested that this may be due to unequal muscular action, the result of the disease.

Dr. J. S. RISIEN RUSSELL.—*Case of myopathy (idiopathic muscular atrophy) coming on late in life.*

T. S., male, aged 46. No similar affection other members of family. Was a coal porter for thirty-three years. Has had "gout." No history of syphilis or lead. Weakness of right arm first noticed after "sunstroke," three and a half years ago. Left arm soon became similarly affected. Gradually worse. Continued at work for eight months. Facies suggestive and orbicularis oris and orbicularis palpebrarum weak, although the defect is not pronounced. Atrophy of muscles about shoulder-girdle and upper arm, together with supinator longus. Deltoids large, but no pronounced pseudo-hypertrophy of any of the muscles. Knee-jerks feeble. No ankle clonus. Plantar reflex normal.

(2) Juvenile Type (Erb).

Dr. J. MICHELL CLARKE.—*Case of juvenile type of muscular atrophy with simultaneous enlargement of parotid glands.*

Frederick E., aged 18. Family history good; no other case in the family. Eldest of five children; the others healthy.

Patient was a well-grown, active, and intelligent boy up to age of 13; the first symptom noticed was that he began to fall about, and could not get up again when he fell. The muscular atrophy was not noticed until he came under observation at the age of 15, but from the fact that weakness began in the legs, and

that his arms were then quite strong, and that he was able to drag himself up by the arms, it is probable the muscular wasting began in the legs. At the same time a slow, painless enlargement of the parotid glands came on, reached a certain size, and then remained stationary. He also became deaf. He has never had mumps or otorrhœa. Since the onset he has either stopped growing or grown very little. No pain or other sensory symptoms throughout.

At the present date the patient is very small and stunted in growth, the head appearing disproportionately large, and this appearance is intensified by a bilateral enlargement of parotid glands, which are soft and elastic and painless. The submaxillary glands are slightly enlarged. The parotid ducts are pervious and the mouth is not dry. The swelling is persistent, and does not alter in size. He is almost completely deaf.

Muscular atrophy is extreme, and, roughly stated, affects R. sterno-mastoid, pectorals, trapezii (lower part), deltoids, triceps, biceps, in a less degree the forearm muscles: latissimus dorsi, intercostals,[1] rectus abdominus external oblique muscles, glutei, to some extent erector spinæ, muscles of thigh, especially quadriceps extensor. The muscles below knee, especially the calf muscles, are less affected. The small muscles of the hands are only slightly affected.

Ocular muscles, and those of the face, unaffected; supra-spinati unaffected (? slightly hypertrophied), infra-spinati and rhomboidei have escaped on one side—partly atrophied on the other. Action of diaphragm feeble.

Electrical reactions show a quantitative reduction proportionate to degree of wasting; deep reflexes show similar reduction or absence. No affection of sensation. The bones of the limbs appear small, but in proportion to arrest of growth of body generally. Absence of subcutaneous fat.

The muscular atrophy has ceased to extend during the last twelve to eighteen months, and there is even some slight improvement in movement.

Dr. J. A. Ormerod.—*Case of myopathy, Erb's juvenile type.*

E. B., aged 22.

No similar disease in family.—The family consisted of patient and a twin brother (healthy) and one other brother.

Present illness.—The first symptom noticed was *at age of* 12,

[1] Upper segments spared, lower two segments departed.

when mother scolded patient for *walking on her toes*. As this did not improve, patient was about *one and a half years later* taken to an orthopædic hospital, where *double tenotomy of both tendon Achilles was performed*. She was given crutches to walk on, but gave up using them six weeks later, as she could not manage them properly *owing to weakness of her arms*. The condition became steadily worse, and at the *age of* 14 she was admitted to the National Hospital. At that time she had double *pes cavus*, *wasting of the shoulder and hip muscles*, and *hypertrophy* of the *lower parts of the deltoids*. Knee-jerks were present. No R. D. *Face normal*. At that time she was *unable to attain the erect position without help*. All hip movements very weak, and general weakness in upper extremities. *Her gait was shuffling and waddling*, but she could walk alone. After leaving hospital she remained in much the same condition for four years, but *at the age of* 18 *she developed almost complete blindness* (light and dark only perceived), and was in the infirmary for seven months, sight recovering completely. Since then she remained much the same, till last year, when her mother noticed increase in size of calves and buttocks.

Present condition. — A sallow, dark-complexioned, well-nourished girl. Intelligent, not emotional. Viscera healthy. *Cranial nerves* and *special senses* good. *No facial affection. Sensation* normal.

Muscles.—Wasting of shoulder, neck and upper arm muscles, especially trapezei, pectorales majores, upper deltoids, biceps, triceps, no wasting of hands. *Wasting of lower erector spinæ and abdominal muscles*. Wasting of *thigh muscles*, especially *vastus externus*. *Hamstrings, rectus*. *Feet shortened, toes squared, pes cavus*. *Hypertrophy* of *infra-spinati* (vertebral borders), *deltoids* (at insertions) ? glutei, *calves*.

Movements.—All shoulder movements affected, especially elevation, abduction and adduction. *Neck* weak. Hands fairly good. Extensors of wrist weak. Flexor and extensors of elbows weak. *Cannot sit* up in bed. Weakness of *lower abdominal recti*. *Cannot attain erect posture*. *Gait:* waddling; tendency to shuffle. Hips: ex. rotation only good movement. Knees: flex. and ext., weak. Ankles: dorsiflexion weak.

Electrical reactions.—F., diminished, or lost, according to muscle wasting, G., diminished, or lost, according to muscle wasting; no polar change.

Reflexes.—Jaw: present. *Arms:* absent. *Knee-jerks:* right, absent; left, just present. *Ankle-jerks:* brisk. *Abd.*: lively.

Plantar: flexor. *Sphincters:* difficulty in starting micturition and constipation.

No loss of light reflex.

Dr. R. HUTCHISON.—*Case of myopathy, Erb's juvenile type.*

F. S., aged 7, had scarlet fever two years ago—never quite recovered, and one year ago had general œdema. Since that time the child has been weak—often falls. The weakness has been progressive, and there is difficulty in raising the arm above the head. The child is intelligent, well nourished. She is poorly developed about the shoulders and upper arms. The fore-arms, hands and lower extremities are well developed. She walks well, and rises from the floor with ease. Movements of the face good. All movements of the upper arm are capable of being performed, but there is weakness of the deltoids, biceps, triceps, the upper portion of the pectoralis major, the serratus magnus and lower portion of the trapezius. All these muscles, however, react readily to faradism and to galvanism. The K.C.C. being greater than the A.C.C. The knee-jerks are active.

(3) Pseudo-hypertrophic Type.

Dr. F. E. BATTEN.—*Myopathy, Pseudo-hypertrophic type.*

William S., aged 9 years and 3 months; fourth child of a family of six—three elder children are girls. Only member affected. No history of similar disease in parents or their relatives. The boy is stated to have been quite well till two years ago, since then he has lost the power of going upstairs. He has become much weaker during the last four months.

Typical case of the pseudo-hypertrophic type of myopathy.

Dr. HEAD.—*A case of pseudo-hypertrophic paralysis in an adult.*

James S. (bootmaker), aged 42. No hereditary history of any nervous disease. One sister only living, but she is healthy.

Mother said he could not stand until he was $2\frac{1}{2}$ years old, nor walk until 3. His walk was peculiar, and not like that of other children, but he was able to go to work, and noticed nothing wrong with him until he was 25 years old; then one day, when walking home from work, he fell down in the street. He then began to notice his arms were getting thinner. From this time onwards the wasting in the arms progressed, and he constantly fell about. He was, however, able to work until 1897, when he

was taken into the Infirmary, where he has remained ever since. He has been a heavy drinker, but there is no history of syphilis.

On examination he presents all the appearances seen in a child with pseudo-hypertrophic paralysis. He rises from the floor by climbing up his thighs in the typical manner. He stands with his belly thrust forward, and waddles as he walks. Calf muscles, the deltoid, supra- and infra-spinati are enlarged and firm; the glutei are very firm but not enlarged. The extensors of the thigh and biceps, pectoralis major, latissimi dorsi are wasted. The knee jerks can just be obtained.

(4) Infantile Type.

Dr. F. E. Batten.—*Three Cases of myopathy, infantile type.*

David S., aged 6. He is the third of a family of four children, the others are said to be healthy. He has never been able to stand or walk. He can sit up but cannot kneel. Talks well and is very intelligent.

Present condition.—The boy is thin and small, unable to walk, unable to stand. In order to cross the room he lies on the floor and rolls round and round on his long axis. He is just able to get into the sitting position.

Muscular development is very small and there is no localised atrophy or hypertrophy. All movements can be performed with the arms. He is unable to extend the legs or the thighs owing to the weakness of the extensor quadriceps, and he cannot flex the thighs or the abdomen. The extensors and flexors of the foot are fairly good and the toes can be moved naturally. The abdominal and dorsal muscles of the back are weak. All movements of the face are well performed.

Electrical reaction.—A contraction can be obtained to a very strong faradic current in most muscles, but no contraction can be obtained in the quadriceps extensor or glutei muscles. The K.C.C. is greater than the A.C.C.

Reflexes.—Knee-jerks absent. Plantars flexor.

Case of myopathy, infantile type.

Samuel T., aged 7. Small baby at birth, legs always contracted, never able to walk. Ninth of eleven children. Only member of the family thus affected. No injury at birth. Brought up on bottle.

Present condition.—Limbs thin and wasted. Bones small. Long hands and feet. Face somewhat expressionless and eyes are prominent, but all facial movements can be performed. He

is unable to walk upright and progresses with knees flexed on thighs. Arms very thin and wasted, muscles small and tough. All movements can be performed and there is no localised wasting or hypertrophy of any muscle. No winging of scapulæ. *Legs* are very thin, the knees cannot be straightened owing to the contraction of the hamstring. Most movements can be performed, but the child cannot extend the legs owing to the contraction of the flexors. Limbs not blue or cold. Knee-jerks absent.

Plantars. — Sometimes extensor, sometimes flexor. All muscles react to a moderately strong faradic current, and the K.C.C. is greater than A.C.C.

Case of myopathy, infantile type.

Condition in 1896.—H. G., aged 6. Stated to be "born exactly like what she is now." Never improved at all.

Has never stood alone, but can move along the floor in sitting position, using her hands to help her. She cannot rise into a sitting position but can sit up if placed in that position. She could always move both legs and could pick up small things with either hand. Can feed herself. Tries to knit and sew. Always lies with the knees partly flexed and her feet bent up on the legs. Mother says she is more intelligent than other children. Talked distinctly at 2 years old. Memory good. Always thin, has not wasted lately. Never any fits. No pain except on one or two occasions in the right knee. No incontinence of urine or fæces. Tenth of eleven children. Full term, breech presentation, feet extended. No instruments. Never any specific fever. Suckled eighteen months.

Family history.—All children alive and healthy. Father healthy. No specific history. No history of paralysis in family.

Present condition.—Very small for her age. Head circumference $19\frac{3}{4}$ inches. Eyes prominent. No palsy. Sits up if placed so, or lies on back with legs flexed. Bones all seem small. No tenderness. No curvature of spine. Feet and hands both appear remarkably long. Knee- and hip-joints cannot be fully extended. Muscular wasting general. Good co-ordination. *Muscular sense* normal. *Sensation* good to all forms. *Sphincters* normal. K.J.'s not obtained. Plantars not obtained. *Special senses.*—Can hear, sees well. Disc clear. Heart, rectum, lungs, liver, &c., normal.

Mental condition.—Child seems backward, probably owing to neglect of education. Answers questions quite sensibly.

(5) Peroneal Type.

Dr. JAMES COLLIER.—*Two cases of peroneal atrophy.*

Two cases of peroneal atrophy from a family of nine children, of whom eight are affected. The atrophy began in the feet just before the age of puberty, and soon after appeared in the intrinsic hand muscles. After progressing for about two years in the hands it ceased, and in the lower extremities it has not progressed in some of the cases for several years. In the youngest member of the family it has become general.

Dr. F. E. BATTEN.—*Typical case of peroneal muscular atrophy.*

F. S., aged 11. When 3 years old the boy had measles, bronchitis and pneumonia, and was very ill. After recovery it was noticed that he dragged the left leg. Seven months later the right leg became affected, and when 6 years old the hands began to lose power.

Patient shows the typical wasting and loss of power in the muscles below the thigh and in the small muscles of the hands.

(6) Anomalous Cases.

Dr. THOMAS BUZZARD.—*Case illustrating an ileo-psoas type of progressive muscular dystrophy.*

E. P., aged 23, female domestic servant, single. Some two years ago noticed difficulty in going upstairs in lifting her foot to the next step above. At first, when the foot had attained its position, she could raise herself on that limb. She continued able to walk well on the flat, but found it difficult when there was the slightest incline. It was about four months ago that she noticed herself tiring easily when walking even on a flat road. In spite of this she was able to walk three miles the evening before admission to hospital without serious discomfort.

Patient had been anæmic for about a year before the onset of her present illness.

At present she has to drag herself upstairs by the banisters and can hardly step up to a footpath from the roadway. She walks quickly on the flat.

Owing to the presence of much subcutaneous fat it is not possible to ascertain exactly the condition of muscular development. There is nothing notable about the condition of the upper extremities, the calf muscles are thought to be relatively small,

but they are firm and knotty. There is no definite wasting to be observed in any part of the lower extremities; the limbs are rounded and the muscles firm.

Her notable difficulties are, first, in raising the foot (either) to a height of a few inches on to a step. In attempting this the limb is rotated outwards, and the foot feebly "flung" up; secondly, difficulty in raising herself on the limb which has thus been brought up. This movement is impossible, except for a low step or foot-stool, and even then is not normally executed. She appears to effect it by bringing forward her centre of gravity by flexing the ankle and knee; she then extends the knee-joint and the other limb is lifted up passively.

In all movements the left limb is slightly stronger than the right. At the hip-joint flexion is weak; extension fair; adduction good; abduction fair; rotation inwards weak; rotation outwards weak. At the knee-joint flexion is very weak; extension good; At the ankle-joint flexion is weak; extension fair; inversion fair; eversion weak. Flexion and extension of the toes are good, and so are the movements of the interossei.

There is no fibrillation, tremor, or inco-ordination, no history of pain, girdle sensation; no spinal deformity. Occasionally numbness and "pins and needles" complained of. No anæsthesia. Some tendency to contracture of the sural muscles; slight degree of pes cavus; lying in bed the feet are generally inverted.

The knee-jerks are obtained with difficulty; Achilles jerk much diminished, just present. No ankle clonus.

Electrical examination.—An extremely strong faradic current fails to bring about any contraction in the hamstrings of either leg. The faradic excitability of all the muscles of the lower extremities is reduced. Galvanic excitability is correspondingly reduced, but there is no polar change. No contraction has been obtained in the hamstrings.

A somewhat expressionless face gives the impression of little intelligence, but patient answers questions well and quickly. The face is rather flat, with little marked furrows, thin lips and cheeks. When asked to show the teeth the mouth is elongated, becoming almond-shaped, without any approach to quadrangular opening at either extremity, the lips being but moderately separated. When the eyes are voluntarily closed as tightly as possible the lids can be separated by the observer with less force than is usual.

Patient is an only child; no like case known in the family.

Dr. F. E. Batten.—*Two cases of muscular atrophy of uncertain origin.*

Case 1.—D. W., boy, aged 7. Was a healthy baby and walked at twelve months. From that time onward progressive wasting of the thighs and weakness of the legs has been noticed. He talked at eighteen months and is very intelligent.

Family history.—He is the sixth of eight children.

(1) Boy, aged 18, healthy. Suckled five months.

(2) Boy, died when 10, had been paralysed since birth. Suckled.

(3) Boy, died when 4. Weakness came on when fourteen months old. Suckled.

(4) Premature birth at eighth month.

(5) Girl, died when 5, paralysed in the legs. Suckled nine months.

(6) Boy, aged 7, patient. Suckled.

(7) Girl, aged 6, healthy. *Not* suckled.

(8) Girl, aged 1½, patient shown. Suckled eleven months.

Present condition.—This boy can just walk, unable to rise from chair or ground. Wasted thighs. Weak dorsal muscles. Small trapezium, atrophy of upper part. Marked weakness of flexors and extensors of the thigh. Weakness of flexors and extensors of knees. Wasting and weakness below the knees is not nearly so marked as above the knee, but considerable weakness of extensors of the foot. Knee-jerks absent. Plantar flexion. No anæsthesia.

Electrical reaction.—No reaction to strong faradic current in affected muscles. Muscles of arm act well.

Case 2.—M. W., girl, aged 1½, sister of above. Wasting of legs first noticed when twelve months old. When six months old was a strong, healthy child. She could stand and "walk up" her mother. Since twelve months old the legs have steadily wasted, and now the child is unable to stand, and is so weak that she moves the legs with the hands.

Present condition.—Intelligent child. Well-developed arms. Wasted and weak thighs and gluteal muscles. Muscles below the knee relatively good. Knee-jerks absent. No anæsthesia.

Dr. James Taylor. — *Case of myopathy with muscular twitching.*

A. W., aged 11. One brother, aged 17, quite healthy. No family history of similar affection. Did not walk till 5½. Has

always walked badly. Difficulty in going upstairs. No sphincter affection. Wasting, especially right shoulder-girdle, also on left side and in lower limbs. Calves firm. Thighs small. Knee-jerks not obtained. Very distinct general twitching in muscles all over body, especially well marked in pectorals. Face looks rather heavy, but no defective movements observed.

The muscular twitching suggests the possible association of spinal cord disease with myopathy.

A Pathological Meeting of the Neurological Society of the United Kingdom was held at 11, Chandos Street, on Thursday, April 2, 1903, at 8.30 p.m.

Dr. E. FARQUHAR BUZZARD read a communication on, and showed specimens in illustration of, "The Pathology and Bacteriology of Landry's Paralysis." (See page 94.)

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EDITOR.